

The Endocrine Society's
CLINICAL | GUIDELINES

Executive Summary
Management of
Thyroid Dysfunction during
Pregnancy and Postpartum:
An Endocrine Society Clinical Practice Guideline



THE JOURNAL OF
CLINICAL
ENDOCRINOLOGY
& METABOLISM

The Endocrine Society's
CLINICAL | GUIDELINES

Executive Summary
Management of
Thyroid Dysfunction during
Pregnancy and Postpartum:
An Endocrine Society Clinical Practice Guideline



THE JOURNAL OF
CLINICAL
ENDOCRINOLOGY
& METABOLISM

Table of Contents

Introduction	4
Methods of Development	4
Background & Evidence	6
Hypothyroidism and Pregnancy: Maternal and Fetal Aspects	7
Management of Maternal Hyperthyroidism: Maternal and Fetal Aspects	8
Gestational Hyperemesis and Hyperthyroidism	9
Autoimmune Thyroid Disease and Miscarriage	9
Thyroid Nodules and Cancer	9
Iodine Nutrition during Pregnancy	10
Postpartum Thyroiditis	10
Screening for Thyroid Dysfunction during Pregnancy	11
References	12
Order Form	15
Reprint Information, Questions & Correspondences	Inside Back Cover

Abstract

Objective: The objective is to provide clinical guidelines for the management of thyroid problems present during pregnancy and in the postpartum.

Participants: The Chair was selected by the Clinical Guidelines Subcommittee (CGS) of The Endocrine Society. The Chair requested participation by the Latin American Thyroid Society, the Asia and Oceania Thyroid Society, the American Thyroid Association, the European Thyroid Association, and the American Association of Clinical Endocrinologists, and each organization appointed a member to the task force. Two members of The Endocrine Society were also asked to participate. The group worked on the guidelines for 2 yrs and held two meetings. There was no corporate funding, and no members received remuneration.

Evidence: Applicable published and peer-reviewed literature of the last two decades was reviewed, with a concentration on original investigations. The grading of evidence was done using the United States Preventive Services Task Force system and, where possible, the GRADE system.

Consensus Process: Consensus was achieved through conference calls, two group meetings, and exchange of many drafts by E-mail. The manuscript was reviewed concurrently by the Society's CGS, Clinical Affairs Committee, members of The Endocrine Society, and members of each of the collaborating societies. Many valuable suggestions were received and incorporated into the final document. Each of the societies endorsed the guidelines.

Conclusions: Management of thyroid diseases during pregnancy requires special considerations because pregnancy induces major changes in thyroid function, and maternal thyroid disease can have adverse effects on the pregnancy and the fetus. Care requires coordination among several healthcare professionals. Avoiding maternal (and fetal) hypothyroidism is of major importance because of potential damage to fetal neural development, an increased incidence of miscarriage, and preterm delivery. Maternal hyperthyroidism and its treatment may be accompanied by coincident problems in fetal thyroid function. Autoimmune thyroid disease is associated with both increased rates of miscarriage, for which the appropriate medical response is uncertain at this time, and postpartum thyroiditis. Fine-needle aspiration cytology should be performed for dominant thyroid nodules discovered in pregnancy. Radioactive isotopes must be avoided during pregnancy and lactation. Universal screening of pregnant women for thyroid disease is not yet supported by adequate studies, but case finding targeted to specific groups of patients who are at increased risk is strongly supported.

J Clin Endocrinol Metab: 92 (8) (Supplement): S1-S47, 2007

INTRODUCTION

Over the past 15 yrs there has been a rapid expansion of knowledge regarding thyroid disease and pregnancy. These advances relate to the optimal management of pregnant women on levothyroxine therapy, the impact of iodine deficiency on the mother and developing fetus, the adverse effect of maternal hypothyroidism on mental development in their infants, the syndrome of postpartum thyroiditis, and its relation to permanent hypothyroidism. Furthermore, a doubling of the miscarriage rate has been reported in studies in antibody-positive euthyroid women, and an increase in preterm delivery has been found in women with subclinical hypothyroidism and/or thyroid autoimmunity.

Given the rapidity of advances in this field, it is not surprising that controversy surrounds optimal detection and management of thyroid disease in the pregnant woman. Thyroid disease during pregnancy has certain characteristics that make writing guidelines more complicated than for some other fields. This field is concerned with the management of pregnant women who may have a variety of known or undisclosed thyroid conditions, such as hypothyroidism and hyperthyroidism, the presence of thyroid auto-antibodies, the presence of nodules, or unsatisfactory iodine nutrition. Pregnancy may affect the course of these thyroid disorders and, conversely, thyroid diseases may affect the course of pregnancy.

Moreover, thyroid disorders (and their management) may affect both the pregnant woman and the developing fetus. Finally, pregnant women may be under the care of multiple health care professionals, including obstetricians, nurse midwives, family practitioners, endocrinologists, and/or internists, making the development of guidelines all the more critical.

METHODS OF DEVELOPMENT

An international task force was created, under the auspices of The Endocrine Society, to review the best evidence in the field and develop evidence-based guidelines. Members of the task force included representatives from The Endocrine Society, American Thyroid Association, Association of American Clinical Endocrinologists, European Thyroid Association, Asia and Oceania Thyroid Association, and the Latin American Thyroid Society. The task force worked during 2 yrs to develop the guidelines, had multiple phone conversations, and two 2-d retreats. Upon completion of the guidelines, they were reviewed and approved by all of the participants.

Our committee undertook to review all material on these topics published in English during the past two decades, or earlier at the working group's discretion. We concentrated on original reports and largely excluded reviews from our references. At present, with the exception of studies on iodide supplementation, only two prospective, randomized intervention trials have been published in this area. We are aware of two large-scale prospective intervention trials that are presently ongoing. Nevertheless, in the last 15 yrs, many high-quality studies have modified older dogmas and profoundly changed the ways in which these patients are managed. These studies are most often prospective or retrospective clinical evaluations of a particular patient population and matched groups of control women. Such studies, when carefully performed, adequately matched, and appropriately interpreted; provide the bulk of the evidence presented herein.

The committee evaluated recommendations and evidence using the methodology of the United States Preventive Service Task Force (USPSTF), in which treatments or medical advice are referred to as a "service." The USPSTF grades its recommendations (level A, B, C, D, or I) on the basis of the strength of evidence and magnitude of net benefit (benefits minus harms), as follows:

A: The USPSTF strongly recommends that clinicians provide (the service) to eligible patients. *The USPSTF found good evidence that (the service) improves important health outcomes and concludes that benefits substantially outweigh harms.*

B: The USPSTF recommends that clinicians provide (the service) to eligible patients. *The USPSTF found at least fair evidence that (the service) improves important health outcomes and concludes that benefits outweigh harms.*

C: The USPSTF makes no recommendation for or against routine provision of (the service). *The USPSTF found at least fair evidence that (the service) can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D: The USPSTF recommends against routinely providing (the service) to asymptomatic patients. *The USPSTF found good evidence that (the service) is ineffective or that harms outweigh benefits.*

I: The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing (the service). *Evidence that (the service) is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.*

The USPSTF grades the quality of the overall evidence for a service on a three-point scale (good, fair, or poor), defined as follows:

Good: Evidence includes consistent results from well designed, well conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

In addition to the USPSTF grading of recommendations, we have also included the appropriate recommendation level as indicated by the GRADE system. The value of an evidence-based recommendation, using the GRADE system, is scored from strong to moderate (1-2) and accompanied by symbols indicating the value of the evidence: high (1, ⊕⊕⊕⊕ or ⊕⊕⊕○), moderate (2, ⊕⊕○○), low (⊕○○○), and very low (○○○○). (There are no equivalents in the GRADE system for the recommendation levels C, D, and I used in the USPSTF system.)

The supporting data for the full committee report is available separately at <http://www.endo-society.org/publications/guidelines/index.cfm> and <http://jcem.endojournals.org/>. The supporting data consists of eight subsections dealing in detail with specific maternal/fetal thyroid problems. Each subsection provides the related background and evidence for recommendations. In the subsection reports, the task force has indicated specific bibliographic citations on which each recommendation is based, and for each report cited as evidence for a given recommendation. We believe that this approach provides an important direct link between the supporting evidence and the recommendation.

BACKGROUND AND EVIDENCE

The complete discussion of background data and evidence is offered in the supporting data that follow this executive summary. Some important issues are noted here.

Pregnant and lactating women require additional iodine intake, whether in iodine-poor or iodine-sufficient countries. The recommended average iodine intake is approximately 250 $\mu\text{g}/\text{d}$ (1). Severe iodine deficiency, if inadequately treated, is a major cause of neurological damage worldwide (2).

Both overt and subclinical hypothyroidism have adverse effects on the course of pregnancy and development of the fetus (3,4,5). Hypothyroidism should be corrected before initiation of pregnancy, replacement dosage should be augmented early in pregnancy (6), and euthyroidism should be maintained throughout. Overt maternal hypothyroidism has been associated with damage to fetal intellectual development (7), presumably because of inadequate transplacental supply of hormone during early pregnancy (8). Whether subclinical hypothyroidism carries this risk remains unproven, but replacement therapy for this condition is nonetheless advised.

Propylthiouracil is recommended as the first-line drug for treatment of hyperthyroidism during pregnancy, because of the probable association of methimazole with fetal developmental abnormalities (9, 10). Maternal Graves' disease, past or present, carries a risk for the pregnancy and for the fetus. Antithyroid drug (ATD) therapy to the mother can induce fetal hypothyroidism, and transplacental passage of TSH-receptor antibodies (TRAb) can cause fetal hyperthyroidism (11,12,13). Targeting ATD treatment to maintain maternal serum free T_4 levels at the upper limit of the nonpregnant T_4 range usually protects the fetus from hypothyroidism (14). Close following of maternal T_4 and TSH levels, assay of TRAb, and fetal ultrasonography including the thyroid are recommended for guiding therapy (15),

and fetal blood sampling is rarely needed (15,16). Fetal hyperthyroidism does not occur during pregnancies in which TRAb levels are normal and ATD is not administered. Surgery may be required in some instances. Propylthiouracil, propranolol, and iodides may be used for preoperative preparation.

Hyperemesis is associated with elevation of thyroid hormone levels above average pregnancy values and suppression of TSH (17,18,19). Occasionally, patients are clinically thyrotoxic. The elevation of thyroid hormone levels and gestational hyperthyroidism are typically self-remitting and in most cases do not require antithyroid treatment (17,20). Subclinical hyperthyroidism, commonly found in this setting, does not require therapy, and therapy is advised against because it might induce fetal hypothyroidism (21).

Thyroid nodules recognized during pregnancy, or growing, are typically biopsied under ultrasound guidance (22,23), and if appropriate, surgery is performed in the mid-trimester (24). Delay in treatment of low-grade tumors until after delivery is not considered a danger (25). Pregnancy is not thought to adversely affect the course of thyroid malignancy (26,27,28). TSH suppression for known thyroid malignancy may be maintained during pregnancy with detectable TSH and with T_4 at the upper end of the range for normal pregnancy. Radioactive iodine (RAI) must not be administered during pregnancy or lactation.

Autoimmune thyroid disease is common in pregnancy. The presence of antibodies to thyroid peroxidase or thyroglobulin is associated with a significant increment in miscarriages (29,30). One prospective study has reported that treatment with T_4 during pregnancy may reverse this risk (31). Additional studies on this important issue are needed.

PPT, a form of autoimmune thyroid disease closely related to Hashimoto's thyroiditis, is found in about 7% of women in the postpartum period (32). It causes hyperthyroidism and/or hypothyroidism that is usually transient (but often seriously symptomatic)

(33,34) and increases the risk of later permanent hypothyroidism (35,36). Although depression may be a symptom of hypothyroidism in any setting, PPT *per se* has not been clearly linked to postpartum depression (37, 38).

A major unsettled question is the advisability of universal screening of pregnant women for thyroid disease, through TSH testing, and possibly antibody testing. The prevalence of overt thyroid disease in this population is 1%, and there is also a 2-3% prevalence of subclinical hypothyroidism and 10-15% antibody positivity (30, 39). As of this date, only one study has demonstrated that treatment of antibody positive euthyroid women with T₄ decreases the rate of miscarriage and preterm delivery (31). Thus, for now, the committee recommends targeted case finding during early pregnancy but anticipates that ongoing studies may alter this recommendation (40). Vaidya *et al.* (41) recently reported a study of screening by means of TSH, T₄, free T₄, and thyroid peroxidase antibodies in 1560 consecutive pregnant women. An important result was that screening only women considered high risk on the basis of a personal or family history of thyroid disease or a history of other autoimmune disease would have missed 30% of women with overt or subclinical hypothyroidism.

RECOMMENDATIONS

1. Hypothyroidism and Pregnancy: Maternal and Fetal Aspects

1.1.1. Both maternal and fetal hypothyroidism are known to have serious adverse effects on the fetus. Therefore maternal hypothyroidism should be avoided. USPSTF recommendation level is A; evidence is fair (GRADE 1 | ⊕⊕⊕○). Targeted case finding is recommended at the first prenatal visit or at diagnosis of pregnancy (see Section 8, *Screening for thyroid dysfunction during pregnancy*). USPSTF recommendation level is B; evidence is fair (GRADE 2 | ⊕⊕○○).

1.1.2. If hypothyroidism has been diagnosed before pregnancy, we recommend adjustment of the preconception thyroxine dose to reach a TSH level not higher than 2.5 μU/mL prior to pregnancy. (USPSTF Recommendation level: I, Evidence-poor). (GRADE 1 | ⊕○○○)

1.1.3. The T₄ dose usually needs to be incremented by 4-6 wk gestation and may require a 30-50% increase in dosage. USPSTF recommendation level is A; evidence is good (GRADE 1 | ⊕⊕⊕⊕).

1.1.4. If overt hypothyroidism is diagnosed during pregnancy, thyroid function tests (TFTs) should be normalized as rapidly as possible. Thyroxine dosage should be titrated to rapidly reach and thereafter maintain serum TSH concentrations of less than 2.5 μU/mL in the first trimester (or 3 μU/mL in the second and third trimester) or to trimester-specific normal TSH ranges. Thyroid function tests should be remeasured within 30-40 days. (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

1.1.5. Women with thyroid autoimmunity who are euthyroid in the early stages of pregnancy are at risk of developing hypothyroidism and should be monitored for elevation of TSH above the normal range. (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕○)

1.1.6. Subclinical hypothyroidism (serum TSH concentration above the upper limit of the reference range with a normal free T₄) has been shown to be associated with an adverse outcome for both the mother and offspring. T₄ treatment has been shown to improve obstetrical outcome but has not been proved to modify long-term neurological development in the offspring. However, given that the potential benefits outweigh the potential risks, the panel recommends T₄ replacement in women with subclinical hypothyroidism. For obstetrical outcome, USPSTF recommendation level is B; evidence is fair (GRADE 1 | ⊕⊕○○). For neurological outcome, USPSTF recommendation level is I; evidence is poor ○○○○

1.1.7. After delivery, most hypothyroid women need a decrease in the thyroxine dosage they received during pregnancy. (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

2. Management of Maternal Hyperthyroidism: Maternal(a) and Fetal Aspects(b)

2.1.a.1. If a subnormal serum TSH concentration is detected during gestation, hyperthyroidism must be distinguished from both normal physiology during pregnancy and hyperemesis gravidarum because of the adverse effects of overt hyperthyroidism on the mother and fetus. Differentiation of Graves' disease from gestational thyrotoxicosis is supported by evidence of autoimmunity, a goiter, and presence of TSH receptor antibodies (TRAb). (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

2.1.a.2. For overt hyperthyroidism due to Graves' disease or hyper-functioning thyroid nodules, antithyroid drug (ATD) therapy should be either initiated (for those with new diagnoses) or adjusted (for those with a prior history) to maintain the maternal thyroid hormone levels for free T₄ in the upper nonpregnant reference range. (USPSTF Recommendation level-A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

2.1.a.3. Because available evidence suggests methimazole may be associated with congenital anomalies, propylthiouracil should be used as a first-line drug, if available, especially during first-trimester organogenesis. Methimazole may be prescribed if propylthiouracil is not available or if a patient cannot tolerate or has an adverse response to propylthiouracil. USPSTF recommendation level is B; evidence is fair (GRADE 1 | ⊕⊕○○).

2.1.a.4. Subtotal thyroidectomy may be indicated during pregnancy as therapy for maternal Graves' disease if (1) a patient has a severe adverse reaction to ATD therapy, (2) persistently high doses of ATD are required, or (3) a patient is not adherent to ATD therapy and has uncontrolled hyperthyroidism. The optimal timing of surgery is in the second trimester. (USPSTF Recommendation level: I, Evidence-poor) (⊕○○○)

2.1.a.5. There is no evidence that treatment of subclinical hyperthyroidism improves pregnancy outcome, and treatment could potentially adversely affect fetal outcome. (USPSTF Recommendation level: I, Evidence-poor) (⊕○○○)

2.1.b.1 TRAb (either TSH receptor-stimulating or -binding antibodies) freely cross the placenta and can stimulate the fetal thyroid. These antibodies should be measured before pregnancy or by the end of the second trimester in mothers with current Graves' disease, with a history of Graves' disease and treatment with ¹³¹I or thyroidectomy, or with a previous neonate with Graves' disease. Women who have a negative TRAb and do not require ATD have a very low risk of fetal or neonatal thyroid dysfunction. USPSTF recommendation level is B; evidence is fair (GRADE 1 | ⊕⊕⊕○).

2.1.b.2. ¹³¹I should not be given to a woman who is or may be pregnant. If inadvertently treated, the patient should be promptly informed of the radiation danger to the fetus, including thyroid destruction if treated after the 12th week of gestation. USPSTF recommendation level is A; evidence is good (GRADE 1 | ⊕⊕⊕⊕). There are no data for or against recommending termination of pregnancy after ¹³¹I exposure. USPSTF recommendation level is I; evidence is poor (⊕○○○)

2.1.b.3. In women with elevated TRAb or in women treated with ATD, fetal ultrasound should be performed to look for evidence of fetal thyroid dysfunction that could include growth restriction, hydrops, presence of goiter, or cardiac failure. (USPSTF Recommendation level: B, Evidence-fair) (GRADE 1 | ⊕⊕⊕○)

2.1.b.4. Umbilical blood sampling should be considered only if the diagnosis of fetal thyroid disease is not reasonably certain from the clinical data and if the information gained would change the treatment. (USPSTF Recommendation level: B, Evidence-fair) (GRADE 1 | ⊕⊕⊕○)

2.1.b.5. All newborns of mothers with Graves' disease should be evaluated for thyroid dysfunction and treated if necessary (USPSTF Recommendation level: B, Evidence-fair) (GRADE 2 | ⊕○○○)

3. Gestational Hyperemesis and Hyperthyroidism

3.1. Thyroid function tests should be measured in all patients with hyperemesis gravidarum (5% weight loss, dehydration, and ketonuria) (USPSTF Recommendation level: B, Evidence-poor) (GRADE 2 | ⊕○○○)

3.2. Few women with hyperemesis gravidarum will require ATD treatment. USPSTF recommendation level is A; evidence is good (GRADE 1 | ⊕⊕⊕⊕). Overt hyperthyroidism believed due to coincident Graves' disease should be treated with ATD. USPSTF recommendation level is B; evidence is fair (GRADE 1 | ⊕⊕⊕○). Gestational hyperthyroidism with clearly elevated thyroid hormone levels (free T₄ above the reference range or total T₄ > 150% of top normal pregnancy value and TSH < 0.1 μU/ml) and evidence of hyperthyroidism may require treatment as long as clinically necessary. USPSTF recommendation level is I; evidence is poor (⊕○○○).

4. Autoimmune Thyroid Disease and Miscarriage

4.1. Although a positive association exists between the presence of thyroid antibodies and pregnancy loss, universal screening for antithyroid antibodies, and possible treatment, can not be recommended at this time. As of this date, only one adequately designed

intervention trial has demonstrated a decrease in the miscarriage rate in thyroid antibody positive euthyroid women (USPSTF Recommendation level: C, Evidence-fair) (GRADE 2 | ⊕○○○)

5. Thyroid Nodules and Cancer

5.1. Fine needle aspiration (FNA) cytology should be performed for thyroid nodules >1 cm discovered in pregnancy. Ultrasound guided FNA may have an advantage for minimizing inadequate sampling. (USPSTF Recommendation level: B; Evidence-fair) (GRADE 1 | ⊕⊕⊕○)

5.2. When nodules are discovered in the first or early second trimester to be malignant on cytopathologic analysis or exhibit rapid growth, pregnancy should not be interrupted but surgery should be offered in the second trimester, before fetal viability. Women found to have cytology indicative of papillary cancer or follicular neoplasm without evidence of advanced disease, which prefer to wait until the postpartum period for definitive surgery, may be reassured that most well-differentiated thyroid cancers are slow growing and that surgical treatment soon after delivery is unlikely to adversely affect prognosis. (USPSTF Recommendation level: B, Evidence-fair) (GRADE 1 | ⊕⊕○○)

5.3. It is appropriate to administer thyroid hormone to achieve a suppressed but detectable TSH in pregnant women with a previously treated thyroid cancer, or an FNA positive for or suspicious for cancer, and those who elect to delay surgical treatment until postpartum. High risk patients may benefit from a greater degree of TSH suppression compared to low risk patients. The free T₄ or total T₄ levels should ideally not be increased above the normal range for pregnancy. (USPSTF Recommendation level: I, Evidence-poor) (⊕○○○)

5.4. RAI administration with ¹³¹I should not be given to women who are breastfeeding. USPSTF recommendation level is B; evidence is fair (GRADE 1 | ⊕⊕⊕⊕). Furthermore, pregnancy should be

avoided for 6 months to 1 yr in women with thyroid cancer who receive therapeutic RAI doses to ensure stability of thyroid function and confirm remission of thyroid cancer. USPSTF recommendation level is B; evidence is fair (GRADE 1 | ⊕⊕○○).

6. Iodine Nutrition during Pregnancy

6.1. Women in the childbearing age should have an average iodine intake of 150 μg per day. During pregnancy and breast-feeding, women should increase their daily iodine intake to 250 μg on average. (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

6.2. Iodine intake during pregnancy and breastfeeding should not exceed twice the daily recommended nutritional intake for iodine, i.e. 500 μg iodine per day. USPSTF recommendation level is I; evidence is poor (⊕○○○).

6.3. To assess the adequacy of the iodine intake during pregnancy in a population, urinary iodine concentration (UIC) should be measured in a cohort of the population. UIC should ideally range between 150 and 250 $\mu\text{g}/\text{L}$. (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

6.4. To reach the daily recommended nutrient intake for iodine, multiple means must be considered, tailored to the iodine intake level in a given population. Different situations must therefore be distinguished: a) countries with iodine sufficiency and/or with a well-established universal salt iodization (USI) program; b) countries without a USI program or an established USI program where the coverage is known to be only partial; and finally c) remote areas with no accessible USI program and difficult socioeconomic conditions. (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

7. Postpartum Thyroiditis

7.1. There are insufficient data to recommend screening of all women for postpartum thyroiditis (PPT) (USPSTF Recommendation level: I, Evidence-poor) (⊕○○○)

7.2. Women known to be thyroid peroxidase antibody positive should have a TSH performed at 3 and 6 months postpartum (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

7.3. The prevalence of PPT in women with type 1 diabetes is threefold greater than in the general population. Postpartum screening (TSH determination) is recommended for women with type 1 diabetes mellitus at 3 and 6 months postpartum (USPSTF Recommendation level: B, Evidence-fair) (GRADE 1 | ⊕⊕○○)

7.4. Women with a history of PPT have a markedly increased risk of developing permanent primary hypothyroidism in the 5- to 10-year period following the episode of PPT. An annual TSH level should be performed in these women (USPSTF Recommendation level: A, Evidence-good) (GRADE 1 | ⊕⊕⊕⊕)

7.5. Asymptomatic women with PPT who have a TSH above the reference range but below 10 $\mu\text{U}/\text{mL}$ and who are not planning a subsequent pregnancy do not necessarily require intervention, but should, if untreated, be re-monitored in 4–8 weeks. Symptomatic women and women with a TSH above normal and who are attempting pregnancy should be treated with levothyroxine. (USPSTF Recommendation level: B, Evidence-fair) (⊕⊕○○)

7.6. There is insufficient evidence to conclude whether an association exists between postpartum depression (PPD) and either PPT or thyroid antibody positivity (in women who did not develop PPT). (USPSTF Recommendation level: I, Evidence-poor) However, as hypothyroidism is a potentially reversible cause of depression, women with postpartum depression should be screened for hypothyroidism and

appropriately treated (USPSTF Recommendation level: B, Evidence-fair) (GRADE 2 | ⊕⊕○○)

8. Screening for Thyroid Dysfunction during Pregnancy

Although the benefits of universal screening for thyroid dysfunction (primarily hypothyroidism) may not be justified by the current evidence (presented above), we recommend case finding among the following groups of women at high risk for thyroid disease by measurement of TSH:

1. Women with a history of hyperthyroid or hypothyroid disease, PPT, or thyroid lobectomy.
2. Women with a family history of thyroid disease.
3. Women with a goiter.
4. Women with thyroid antibodies (when known).
5. Women with symptoms or clinical signs suggestive of thyroid underfunction or overfunction, including anemia, elevated cholesterol, and hyponatremia.
6. Women with type I diabetes.
7. Women with other autoimmune disorders.
8. Women with infertility who should have screening with TSH as part of their infertility work-up.
9. Women with previous therapeutic head or neck irradiation.
10. Women with a history of miscarriage or preterm delivery. USPSTF recommendation level is B; evidence is fair (GRADE 1 | ⊕⊕○○).

References

1. **World Health Organization**, Technical consultation of experts in Geneva in January 2005. The prevention and control of iodine deficiency in pregnant and lactating women and in children under two years: recommendations of a WHO Technical Consultation. *Public Health Nutr*, in press
2. **Bleichrodt N, Born M** 1994 A meta-analysis of research on iodine and its relationship to cognitive development. In: Stanbury JB, ed. *The damaged brain of iodine deficiency: cognitive, behavioral, neuromotor, educative aspects*. New York: Cognizant Communication; 195-200
3. **Davis LE, Leveno KJ, Cunningham FG** 1988 Hypothyroidism complicating pregnancy. *Obstet Gynecol* 72:108-112
4. **Leung AS, Millar LK, Koonings PP, Montoro M, Mestman JH** 1993 Perinatal outcome in hypothyroid pregnancies. *Obstet Gynecol* 81:349-353
5. **Wasserstrum N, Anania CA** 1995 Perinatal consequences of maternal hypothyroidism in early pregnancy and inadequate replacement. *Clin Endocrinol (Oxf)* 42:353-358
6. **Alexander EK, Marqusee E, Lawrence J, Jarolim P, Fischer GA, Larsen R** 2004 Timing and magnitude of increases in levothyroxine requirements during pregnancy in women with hypothyroidism. *N Engl J Med* 351:241-249
7. **Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell ML, Hermos RJ, Waisbren SE, Faix JD, Klein RZ** 1999 Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med* 341:549-555
8. **Kester MH, Martinez de Mena R, Obregon MJ, Marinkovic D, Howatson A, Visser TJ, Hume R, Morreale de Escobar G** 2004 Iodothyronine levels in the human developing brain: major regulatory roles of iodothyronine deiodinases in different areas. *J Clin Endocrinol Metab* 89:3117-3128
9. **Clementi M, Di Gianantonio E, Pelo E, Mammi I, Basile RT, Tenconi R** 1999 Methimazole embryopathy: delineation of the phenotype. *Am J Med Genet* 83:43-46
10. **Johnsson E, Larsson G, Ljunggren M** 1997 Severe malformations in infant born to hyperthyroid woman on methimazole. *Lancet* 350:1520
11. **Peleg D, Cada S, Peleg A, Ben-Ami M** 2002 The relationship between maternal serum thyroid-stimulating immunoglobulin and fetal and neonatal thyrotoxicosis. *Obstet Gynecol* 99:1040-1043
12. **Weetman AP** 2000 Graves' disease. *N Engl J Med* 343:1236-1248
13. **McKenzie JM, Zakarija M** 1992 Fetal and neonatal hyperthyroidism and hypothyroidism due to maternal TSH receptor antibodies. *Thyroid* 2:155-159
14. **Momotani N, Noh JY, Ishikawa N, Ito K** 1997 Effects of propylthiouracil and methimazole on fetal thyroid status in mothers with Graves' hyperthyroidism. *J Clin Endocrinol Metab* 82:3633-3636
15. **Luton D, Le Gac I, Vuillard E, Castanet M, Guibourdenche J, Noel M, Toubert ME, Leger J, Boissinot C, Schlageter MH, Garel C, Tebeka B, Oury JF, Czernichow P, Polak M** 2005 Management of Graves' disease during pregnancy: the key role of fetal thyroid gland monitoring. *J Clin Endocrinol Metab* 90:6093-6098
16. **Laurberg P, Nygaard B, Glinoe D, Grussendorf M, Orgiazzi J** 1998 Guidelines for TSH-receptor antibody measurements in pregnancy: results of an evidence-based symposium organized by the European Thyroid Association. *Eur J Endocrinol* 139:584-586
17. **Goodwin TM, Montoro M, Mestman JH** 1992 Transient hyperthyroidism and hyperemesis gravidarum: clinical aspects. *Am J Obstet Gynecol* 167:648-652
18. **Al-Yatama M, Diejomaoh M, Nandakumaran M, Monem RA, Omu AE, Al Kandari F** 2002 Hormone profile of Kuwaiti women with hyperemesis gravidarum. *Arch Gynecol Obstet* 266:218-222
19. **Leylek OA, Cetin A, Toyaksi M, Erselcan T** 1996 Hyperthyroidism in hyperemesis gravidarum. *Int J Gynaecol Obstet* 55:33-37
20. **Tan JY, Loh KC, Yeo GS, Chee YC** 2002 Transient hyperthyroidism of hyperemesis gravidarum. *BJOG* 109:683-688
21. **Casey BM, Dashe JS, Wells CE, McIntire DD, Leveno KJ, Cunningham FG** 2006 Subclinical hyperthyroidism and pregnancy outcomes. *Obstet Gynecol* 107:337-341
22. **Choe W, McDougall IR** 1994 Thyroid cancer in pregnant women: diagnostic and therapeutic management. *Thyroid* 4:433-435

23. **Rosen IB, Korman M, Walfish PG** 1997 Thyroid nodular disease in pregnancy: current diagnosis and management. *Clin Obstet Gynecol* 40:81-89
24. **Sam S, Molitch ME** 2003 Timing and special concerns regarding endocrine surgery during pregnancy. *Endocrinol Metab Clin North Am* 32:337-354
25. **Doherty CM, Shindo ML, Rice DH, Montero M, Mestman JH** 1995 Management of thyroid nodules during pregnancy. *Laryngoscope* 105:251-255
26. **Moosa M, Mazzaferri EL** 1997 Outcome of differentiated thyroid cancer diagnosed in pregnant women. *J Clin Endocrinol Metab* 82:2862-2866
27. **Herzon FS, Morris DM, Segal MN, Rauch G, Parnell T** 1994 Coexistent thyroid cancer and pregnancy. *Arch Otolaryngol Head Neck Surg* 120:1191-1193
28. **Schlumberger M, De Vathaire F, Ceccarelli C, Francese C, Pinchera A, Parmentier C** 1995 Outcome of pregnancy in women with thyroid carcinoma. *J Endocrinol Invest* 18:150-151
29. **Glinoe D, Soto MF, Bourdoux P, Lejeune B, Delange F, Lemone M, Kinthaert J, Robijn C, Grun JP, de Nayer P** 1991 Pregnancy in patients with mild thyroid abnormalities: maternal and neonatal repercussions. *J Clin Endocrinol Metab* 73:421-427
30. **Stagnaro-Green A, Roman SH, Cobin RH, el-Harazy E, Alvarez-Marfany M, Davies TF** 1990 Detection of at-risk pregnancy by means of highly sensitive assays for thyroid autoantibodies. *JAMA* 264:1422-1425
31. **Negro R, Formoso G, Mangieri T, Pezzarossa A, Dazzi D, Hassan H** 2006 Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: effects on obstetrical complications. *J Clin Endocrinol Metab* 91:2587-2591
32. **Amino N, Tada H, Hidaka Y** 1999 Postpartum autoimmune thyroid syndrome: a model of aggravation of autoimmune disease. *Thyroid* 9:705-713
33. **Stagnaro-Green A** 2002 Postpartum thyroiditis. *J Clin Endocrinol Metab* 87:4042-4047
34. **Lucas A, Pizarro E, Granada ML, Salinas I, Foz M, Sanmarti A** 2000 Postpartum thyroiditis: epidemiology and clinical evolution in a nonselected population. *Thyroid* 10:71-77
35. **Othman S, Phillips DI, Parkes AB, Richards CJ, Harris B, Fung H, Darke C, John R, Hall R, Lazarus JH** 1990 A long-term follow-up of postpartum thyroiditis. *Clin Endocrinol (Oxf)* 32:559-564
36. **Tachi J, Amino N, Tamaki H, Aozasa M, Iwatani Y, Miyai K** 1988 Long term follow-up and HLA association in patients with postpartum hypothyroidism. *J Clin Endocrinol Metab* 66:480-484
37. **Kent GN, Stuckey BG, Allen JR, Lambert T, Gee V** 1999 Postpartum thyroid dysfunction: clinical assessment and relationship to psychiatric affective morbidity. *Clin Endocrinol (Oxf)* 51:429-438
38. **Lucas A, Pizarro E, Granada ML, Salinas I, Sanmarti A** 2001 Postpartum thyroid dysfunction and postpartum depression: are they two linked disorders? *Clin Endocrinol (Oxf)* 55:809-814
39. **Allan WC, Haddow JE, Palomaki GE, Williams JR, Mitchell ML, Hermos RJ, Faix JD, Klein RZ** 2000 Maternal thyroid deficiency and pregnancy complications: implications for population screening. *J Med Screen* 7:127-130
40. **Lazarus JH, Premawardhana LD** 2005 Screening for thyroid disease in pregnancy. *J Clin Pathol* 58:449-452
41. **Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchinson S, and Bilous R** 2007 Detection of thyroid dysfunction in early pregnancy: universal screening or targeted high-risk case finding. *J Clin Endocrinol Metab* 92:203-207



8401 Connecticut Avenue, Suite 900
 Chevy Chase, MD 20815-5817
 Phone (301) 941-0210; Fax (301) 941-0257
 societyservices@endo-society.org
 FEIN 73-0521256

THE ENDOCRINE SOCIETY GUIDELINE ORDER FORM

(Single reprint request for orders of 100 and less)

PRODUCTS	QTY.	PRICE (USD)		SUBTOTAL
		Member	Non-Member	
Androgen Therapy in Women: An Endocrine Society Clinical Practice Guideline		\$15.00	\$20.00	
Evaluation & Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline		\$15.00	\$20.00	
Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline		Executive Summary (MMTD07)—\$10.00 Guideline (MTSD07)—\$10.00	Executive Summary (MMTD07)—\$15.00 Guideline (MTSD07)—\$15.00	
Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline		\$15.00	\$20.00	
Miscellaneous				
TOTAL		All prices include sales tax		\$

PAYMENT INFORMATION: Check MasterCard Visa

Card Number _____ Expiration Date _____

Billing Address _____ Signature _____

Are you a member of The Endocrine Society? Yes No

If you are a member and you know your member ID, please provide: _____

Prefix:	First Name (Given):	Middle:	Last (Surname):
Institution/Company:		Dept/Div:	
Street/PO:			
City:		State/Province:	Zip/Mail Code: Country:
Telephone:		Fax:	Email:
Degree(s) that you would like listed after your name:		Professional Title:	Date of Birth: Gender: <input type="radio"/> Male <input type="radio"/> Female
Which of the following best describes your primary professional role? (Please mark only one)		Race or Ethnic Affiliation (voluntary)	
<input type="radio"/> Administrator <input type="radio"/> Retired <input type="radio"/> Basic Researcher <input type="radio"/> Teacher/Educator <input type="radio"/> Clinical Practitioner <input type="radio"/> Fellow (Clinical) <input type="radio"/> Clinical Researcher <input type="radio"/> Fellow (Postdoctoral/Research) <input type="radio"/> Industry/Corporate Professional <input type="radio"/> Student <input type="radio"/> Nurse/Healthcare Professional <input type="radio"/> Other _____		<input type="radio"/> African American, Black <input type="radio"/> Asian <input type="radio"/> Hispanic <input type="radio"/> Native American, Eskimo, Aleut <input type="radio"/> Pacific Islander <input type="radio"/> White, Caucasian <input type="radio"/> Other _____	

What goes into our Clinical Guidelines *is a story worth telling*

The extensive process that goes into creating The Endocrine Society's Clinical Guidelines not only provides validation and assurance, but also raises the standard for the development of guidelines everywhere.

The guidelines are developed using a multi-step process that reflects the standards of excellence embraced by The Endocrine Society.

Endocrine Society Clinical Guidelines Now Available:

*Evaluation and Treatment of
Adult Growth Hormone Deficiency
Testosterone Therapy in Adult Men with
Androgen Deficiency Syndromes
Androgen Therapy in Women*

Endocrine Society Clinical Guidelines Coming Soon:

1. Continuous Glucose Monitoring
2. Cushing's Syndrome
3. Diagnosis and Evaluation of Women with Hirsutism
4. Lipids (with an endocrine focus)
5. Management of Adult Hypoglycemic Disorders
6. Metabolic Syndrome
7. Prevention and Treatment of Pediatric Obesity
8. Primary Aldosteronism
9. Treatment of Persons with Transsexualism
10. Vitamin D & Bone



To view patient guides (companion pieces to the clinical guidelines), visit The Hormone Foundation's Web site at www.hormone.org/public/patientguides.cfm.



Commercial Reprint Information

For information on reprint requests of more than 101 and commercial reprints contact:

Heather Edwards
Reprint Sales Specialist
Cadmus Professional Communications

Phone: 410.691.6214
Fax: 410.684.2789
Email: endoreprints@cadmus.com

Single Reprint Information

For information on reprints of 100 and fewer, complete the guideline order form and return using one of the following methods:

Mail: The Endocrine Society
c/o Bank of America
P.O. Box 630721
Baltimore, MD 21263-0736

Fax: 301.941.0257
Email: Societyservices@endo-society.org

Questions & Correspondences

The Endocrine Society
Attn: Government & Public Affairs Department
8401 Connecticut Avenue, Suite 900
Chevy Chase, MD 20815

Phone: 301.941.0200
Email: govt-prof@endo-society.org
Web: www.endo-society.org

For more information on The Endocrine Society's Clinical Practice Guidelines or to download the complete version of this guideline, visit <http://www.endo-society.org/publications/guidelines/index.cfm>.



The Endocrine Society
8401 Connecticut Avenue, Suite 900
Chevy Chase, MD 20815

301.941.0200
www.endo-society.org