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Thyroid Disease in Pregnancy

Because thyroid disease is the second most common endocrine disease affecting women of reproductive age, obstetricians often care for patients who have been previously diagnosed with alterations in thyroid gland function. In addition, both hyperthyroidism and hypothyroidism may initially manifest during pregnancy. Obstetric conditions, such as gestational trophoblastic disease or hyperemesis gravidarum, may themselves affect thyroid gland function. This document will review the thyroid-related pathophysiologic changes created by pregnancy and the maternal–fetal impact of thyroid disease.

This Practice Bulletin was developed by the ACOG Committee on Practice Bulletins—Obstetrics with the assistance of Sarah Kilpatrick, MD, PhD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

Reaffirmed 2008

Background

Definitions

Thyrotoxicosis is the clinical and biochemical state that results from an excess production of and exposure to thyroid hormone from any etiology. In contrast, hyperthyroidism is thyrotoxicosis caused by hyperfunctioning of the thyroid gland (1). Graves' disease is an autoimmune disease characterized by production of thyroid-stimulating immunoglobulin (TSI) and thyroid-stimulating hormone-binding inhibitory immunoglobulin (TBII) that act on the thyroid-stimulating hormone (TSH) receptor to mediate thyroid stimulation or inhibition, respectively. Thyroid storm is characterized by a severe, acute exacerbation of the signs and symptoms of hyperthyroidism.

Hypothyroidism is caused by inadequate thyroid hormone production. Postpartum thyroiditis is an autoimmune inflammation of the thyroid gland that presents as new-onset, painless hypothyroidism, transient thyrotoxicosis, or thyrotoxicosis followed by hypothyroidism within 1 year postpartum.

Physiologic Changes in Thyroid Function During Pregnancy

Table 1 depicts how thyroid function test (TFT) results change in normal pregnancy and in hyperthyroid and hypothyroid states. The concentration of thyroid binding globulin (TBG) increases in pregnancy because of reduced hepatic clearance and estrogenic stimulation of TBG synthesis (2). The test results that change significantly in pregnancy are those that are influenced by serum TBG concentration. These tests include total thyroxine (TT_4), total triiodothyronine (TT_3), and resin triiodothyronine uptake (RT_3U). Although there may be a transient increase in free thyroxine (FT_4) and free thyroxine index (FTI) in the first trimester (possibly related to human chorionic gonadotropin [hCG] stimulation), this increase does not result in elevations beyond the normal nonpregnant range (3).

Plasma iodide levels decrease during pregnancy because of fetal use of iodide and increased maternal renal clearance of iodide (2). This alteration is associated with a noticeable increase in thyroid gland size in approximately 15% of women (2, 4). In two longitudinal studies of more than 600 women without thyroid disease, thyroid volume, measured by ultrasonography, significantly increased in pregnancy (with a mean increase in size of 18% that was noticeable in most women) and returned to normal in the postpartum period (4, 5). None of these women had abnormal TFT results despite their enlarged thyroid glands.

Thyroid Function and the Fetus

The fetal thyroid begins concentrating iodine at 10–12 weeks of gestation and is controlled by pituitary TSH by approximately 20 weeks of gestation. Fetal serum levels of TSH, TBG, FT_4, and free triiodothyronine (FT_3) increase throughout gestation, reaching mean adult levels at approximately 36 weeks of gestation (6). Thyroid-stimulating hormone does not cross the placenta, and only small amounts of thyroxine (T_4) and triiodothyronine (T_3) cross the placenta. In neonates with congenital hypothyroidism, enough maternal thyroid hormone crosses the placenta to prevent the overt stigmata of hypothyroidism at birth and maintain cord blood thyroid hormone levels at 25–50% of normal (7). However, thyrotropin-releasing hormone (TRH), iodine, and TSH receptor immunoglobulins do cross the placenta, as do the thioamides propylthiouracil (PTU) and methimazole.

Hyperthyroidism

Signs and Symptoms

Hyperthyroidism occurs in 0.2% of pregnancies; Graves' disease accounts for 95% of these cases (8). The signs and symptoms of hyperthyroidism include nervousness, tremors, tachycardia, frequent stools, excessive sweating, heat intolerance, weight loss, goiter, insomnia, palpitations, and hypertension. Distinctive symptoms of Graves' disease are ophthalmopathy (signs including lid lag and lid retraction) and dermopathy (signs include localized or pretibial myxedema). Although some symptoms of hyperthyroidism are similar to symptoms of pregnancy or nonthyroid disease, serum TFTs differentiate thyroid disease from nonthyroid disease.

Inadequately treated maternal thyrotoxicosis is associated with a greater risk of preterm delivery, severe preeclampsia, and heart failure than treated, controlled maternal thyrotoxicosis (9, 10). Although untreated hyperthyroidism has been associated with miscarriage (8, 11), it is difficult to find concrete data to support this claim.

Fetal and Neonatal Effects

Inadequately treated hyperthyroidism also is associated with an increase in medically indicated preterm deliveries, low birth weight (LBW), and possibly fetal loss (9, 10). In one study, all of seven fetal losses occurred in women with persistent hyperthyroidism (9).

Fetal and neonatal risks associated with Graves' disease are related either to the disease itself or to thioamide treatment of the disease. The possibility of fetal thyrotoxicosis should be considered in all women with a

Table 1. Changes in Thyroid Function Test Results in Normal Pregnancy and in Thyroid Disease

Maternal Status	TSH	FT_4	FTI	TT_4	TT_3	RT_3U
Pregnancy	No change	No change	No change	Increase	Increase	Decrease
Hyperthyroidism	Decrease	Increase	Increase	Increase	Increase or no change	Increase
Hypothyroidism	Increase	Decrease	Decrease	Decrease	Decrease or no change	Decrease

Abbreviations: TSH, thyroid-stimulating hormone; FT_4, free thyroxine; FTI, free thyroxine index; TT_4, total thyroxine; TT_3, total triiodothyronine; RT_3U, resin T3 uptake.

history of Graves' disease (8). If fetal thyrotoxicosis is diagnosed, consultation with a clinician with expertise in such conditions is warranted.

Because a large proportion of thyroid dysfunction in women is mediated by antibodies that cross the placenta (Graves' disease and chronic autoimmune thyroiditis), there is a legitimate concern for risk of immune-mediated hypothyroidism and hyperthyroidism to develop in the neonate. Women with Graves' disease have TSI and TBII that can stimulate or inhibit the fetal thyroid. The latter (TBII) may cause transient hypothyroidism in neonates of women with Graves' disease (12, 13). One to five percent of these neonates have hyperthyroidism or neonatal Graves' disease caused by the transplacental passage of maternal TSI (11). The incidence is low because of the balance of stimulatory and inhibitory antibodies with thioamide treatment (14). Maternal antibodies are cleared less rapidly than thioamides in the neonate, resulting in a sometimes delayed presentation of neonatal Graves' disease (14). The incidence of neonatal Graves' disease is unrelated to maternal thyroid function. The neonates of women who have been treated surgically or with radioactive iodine 131 (I-131) prior to pregnancy and require no thioamide treatment are at higher risk for neonatal Graves' disease because they lack suppressive thioamide (14).

Etiology and Differential Diagnosis

The most common cause of hyperthyroidism is Graves' disease. The other clinical characteristics of Graves' disease also are immune-mediated but they are less understood. The diagnosis of Graves' disease is generally made by documenting elevated levels of FT_4 or an elevated FTI, with suppressed TSH in the absence of a nodular goiter or thyroid mass. Although most patients with Graves' disease have TSH receptor, antimicrosomal, or antithyroid peroxidase antibodies, measurement of these is neither required nor recommended to establish the diagnosis (11). Other etiologies of thyrotoxicosis are excess production of TSH, gestational trophoblastic neoplasia, hyperfunctioning thyroid adenoma, toxic multinodular goiter, subacute thyroiditis, and extrathyroid source of thyroid hormone.

Hypothyroidism

It is well accepted that having one autoimmune disease increases the likelihood of developing another; autoimmune thyroid dysfunction is no exception. For example, there is a 5–8% incidence of hypothyroid disease in patients with type 1 (insulin-dependent) diabetes (15). Women with type 1 diabetes also have a 25% risk of developing postpartum thyroid dysfunction (15).

Signs and Symptoms

The classic signs and symptoms of hypothyroidism are fatigue, constipation, intolerance to cold, muscle cramps, hair loss, dry skin, prolonged relaxation phase of deep tendon reflexes, and carpal tunnel syndrome. These are initially indolent and nonspecific but may progress to weight gain, intellectual slowness, voice changes, and insomnia. If left untreated, hypothyroidism will progress to myxedema and myxedema coma. It is unusual for advanced hypothyroidism to present in pregnancy. Subclinical hypothyroidism is defined as elevated TSH with normal FTI in an asymptomatic patient. Untreated hypothyroidism is associated with an increased risk of preeclampsia, but it is not clear from the available data whether subclinical hypothyroidism carries a similar risk (16, 17).

Fetal and Neonatal Effects

In retrospective studies, a high incidence of LBW in neonates was associated with inadequately treated hypothyroidism (16, 17). The etiology of LBW in these studies was preterm delivery (medically indicated), preeclampsia, or placental abruption. One study reported two stillbirths, both of which were associated with placental abruption and preeclampsia (17). It is not clear whether hypothyroidism is associated with intrauterine growth restriction independent of other complications. Women with iodine-deficient hypothyroidism are at significant risk of having babies with congenital cretinism (growth failure, mental retardation, and other neuropsychologic deficits). In an iodine-deficient population, treatment with iodine in the first and second trimesters of pregnancy significantly reduces the incidence of the neurologic abnormalities of cretinism (18).

Untreated congenital hypothyroidism also results in cretinism. The incidence of congenital hypothyroidism is 1 per 4,000 newborns, and only 5% of neonates are identified by clinical symptoms at birth, likely because of the ameliorative effects of maternal thyroid hormone (2). All 50 states and the District of Columbia offer screening of newborns for congenital hypothyroidism. If identified and treated within the first few weeks of life, near-normal growth and intelligence can be expected (19).

Etiology and Differential Diagnosis

Most cases of hypothyroidism are the result of a primary thyroid abnormality; a small number of cases are caused by hypothalamic dysfunction. The most common etiologies of hypothyroidism in pregnant or postpartum women are Hashimoto's disease (chronic thyroiditis or chronic autoimmune thyroiditis) (1), subacute thyroidi-

tis, thyroidectomy, radioactive iodine treatment, and iodine deficiency. In developed countries, Hashimoto's disease is the most common etiology (20) and is characterized by the production of antithyroid antibodies, including thyroid antimicrosomal and antithyroglobulin antibodies. Both Hashimoto's disease and iodine deficiency are associated with goiter (a sign of compensatory TSH production), while subacute thyroiditis is not associated with goiter.

Worldwide, the most common cause of hypothyroidism is iodine deficiency (8). Although iodine deficiency is rare in the United States, some populations may benefit from consideration of this etiology of hypothyroidism, including certain immigrant populations and those with poor nutrition.

Clinical Considerations and Recommendations

▶ *What laboratory tests are used to diagnose and manage thyroid disease during pregnancy?*

The mainstay of thyroid function evaluation is TSH testing; such testing is now performed using monoclonal antibodies, making it more sensitive than the original radioimmunoassay. The American Association of Clinical Endocrinologists (21) and the American Thyroid Association (22) recommend TSH testing as the initial test for the screening and evaluation of symptomatic disease for all men and women. The free component is the biologically active portion and is not subject to change in conditions that alter TBG, such as pregnancy. In a pregnant patient suspected of being hyperthyroid or hypothyroid, TSH and FT_4 or FTI should be measured. Free thyroxine assessment by either direct immunoradiometric or chemiluminescent methods generally is available and preferred over the equilibrium dialysis method. However, FTI can be calculated as the product of TT_4 and RT_3U if FT_4 is not available. Measurement of FT_3 usually is only pursued in patients with thyrotoxicosis with suppressed TSH but normal FT_4 measurements. Elevated FT_3 indicates T_3 toxicosis, which may occur before excessive FT_4 production develops (11, 23).

Another test of thyroid function is the TRH stimulation test, which evaluates the secretory ability of the pituitary. The various antibody tests include TSH receptor antibodies, which can be either stimulatory (TSI) or inhibitory (TBII), and antimicrosomal antibodies. The usefulness of these various antibodies in pregnancy is complex and will be discussed as follows.

Although the incidence of neonatal Graves' disease is associated with extremely high levels of maternal TSI, the clinical usefulness of evaluating these levels is not clear. In general, perinatal experts suggest there is no practical use for measuring TSI routinely (8), while endocrinologists suggest that measuring TSI in the third trimester is useful (11, 14, 24, 25). Routine evaluation of maternal TSI levels is not recommended, but such evaluation may be helpful in some circumstances.

▶ *What medications can be used to treat hyperthyroidism and hypothyroidism in pregnancy, and how should they be administered and adjusted during pregnancy?*

Hyperthyroidism in pregnancy is treated with thioamides, specifically PTU and methimazole, which decrease thyroid hormone synthesis by blocking the organification of iodide. Propylthiouracil also reduces the peripheral conversion of T_4 to T_3 and, thus, may have a quicker suppressant effect than methimazole. Traditionally, PTU has been preferred in pregnant patients because it was believed that PTU crossed the placenta less well than methimazole and because methimazole was associated with fetal aplasia cutis, a congenital skin defect of the scalp (26). However, recent data have refuted both of these arguments. One study comparing FT_4 and TSH in newborn umbilical cord blood samples of women treated with PTU with those of women treated with methimazole found no significant difference in mean FT_4 or TSH levels. Furthermore, there was no relationship between maternal dosage of thioamide and umbilical cord blood levels of TSH or FT_4 (27). A retrospective study that compared 99 women treated with PTU with 36 women treated with methimazole reported no cases of aplasia cutis and similar rates of fetal anomalies (3%) (28). Finally, there was no significant difference in the incidence of aplasia cutis between control women without thyroid disease and women with hyperthyroidism who were treated with methimazole (26).

Thioamide treatment of Graves' disease can suppress fetal and neonatal thyroid function. However, it usually is transient and rarely requires therapy. Fetal goiter also has been associated with thioamide treatment for Graves' disease, presumably caused by drug-induced fetal hypothyroidism (29). Fetal thyrotoxicosis secondary to maternal antibodies is rare, but all fetuses of women with Graves' disease should be monitored for appropriate growth and normal heart rate. However, in the absence of these findings, routine screening for fetal goiter by ultrasonography is unnecessary. All neonates of women with thyroid disease are at risk for neonatal thyroid dysfunction, and the neonate's pediatrician should be aware of the maternal diagnosis.

Women taking PTU may breastfeed because only small amounts of the medication cross into breast milk. Studies have demonstrated that TFT results were normal in neonates after 1–8 months of breastfeeding from women taking PTU (30, 31). Methimazole also is considered safe for breastfeeding; however, it is present in a higher ratio in breast milk (30).

The goal of management of hyperthyroidism in pregnancy is to maintain the FT_4 or FTI in the high normal range using the lowest possible dosage of thioamides to minimize fetal exposure to thioamides. Thus, once treatment has started, it may be helpful to measure FT_4 or FTI every 2–4 weeks and titrate the thioamide until FT_4 or FTI are consistently in the high normal range (8). In more than 90% of patients, improvement will be seen within 2–4 weeks after thioamide treatment begins (11).

One side effect of thioamides is agranulocytosis. The incidence of agranulocytosis is 0.1–0.4%; it usually presents with a fever and sore throat. If a patient on thioamides develops these symptoms, a complete blood cell count should be drawn and the medication should be discontinued. Treatment with the other thioamide carries a significant risk of cross reaction. Other major side effects of thioamides, including thrombocytopenia, hepatitis, and vasculitis, occur in less than 1% of patients; minor side effects, including rash, nausea, arthritis, anorexia, fever, and loss of taste or smell, occur in 5% of patients (11).

Beta-blockers may be used during pregnancy to ameliorate the symptoms of thyrotoxicosis until thioamides decrease thyroid hormone levels. Propranolol is the most common β-blocker used for this indication. Thyroidectomy should be reserved for women in whom thioamide treatment is unsuccessful.

Iodine 131 is contraindicated in pregnant women because of the risk of fetal thyroid ablation; therefore, women should avoid pregnancy for 4 months after I-131 treatment (23). Unfortunately, our understanding of fetal thyroid ablation and the consequent risk of fetal hypothyroidism from exposure to maternal I-131 comes from the inadvertent treatment of pregnant women (32, 33). Counseling of women exposed to I-131 in pregnancy should focus on the gestational age at exposure. If the woman was at less than 10 weeks of gestation when exposed to I-131, it is unlikely the fetal thyroid was ablated. If exposure occurred at 10 weeks of gestation or later, the woman must consider the risks of induced congenital hypothyroidism and consider whether to continue the pregnancy. Breastfeeding should be avoided for at least 120 days after treatment with I-131 (34).

Treatment of hypothyroidism in pregnant women is the same as for nonpregnant women and involves administering levothyroxine at sufficient dosages to normalize TSH levels. It takes approximately 4 weeks for the thyroxine therapy to alter the TSH level. Therefore, levothyroxine therapy should be adjusted at 4-week intervals until TSH levels are stable. Data indicate pregnancy increases maternal thyroid hormone requirements in women with hypothyroidism diagnosed before pregnancy (2, 35). In these studies, TSH levels increased while FTI decreased during pregnancy in these women, necessitating an increase in mean thyroxine dosage from 0.1 mg/day before pregnancy to 0.148 mg/day during pregnancy (35). In stable patients, it is prudent to check TSH levels every trimester in pregnant women with hypothyroidism (21).

▶ *What changes in thyroid function occur with hyperemesis gravidarum, and should TFTs be performed routinely in women with hyperemesis?*

Nausea and vomiting of pregnancy have been attributed to the high hCG levels in the first trimester, and women with hyperemesis gravidarum have been assumed to have particularly high hCG levels and to be at risk for hyperthyroidism. In a prospective study of 67 women with singleton pregnancies and hyperemesis, 66% were found to have biochemical hyperthyroidism with an undetectable level of TSH or elevated FTI or both (36). The biochemical hyperthyroidism resolved in all of the women without treatment by 18 weeks of gestation (36). Further, the women with the most severe hyperemesis had significantly higher FTIs than those with mild or moderate disease.

Complete resolution of biochemical and clinical hyperthyroidism also has been reported in other studies (37, 38). These studies have reported that some women with hyperemesis gravidarum required a short course of thioamides; however, most of these women had resolution of their signs and symptoms without treatment (38, 39). Women who required treatment throughout the remainder of their pregnancies had other symptoms of thyroid disease, including thyroid enlargement, persistent tachycardia despite fluid replacement, and abnormal response to TRH stimulation (39). In a study comparing pregnant women with hyperemesis and those without hyperemesis, there was no difference in mean TSH or FT_3 levels (40). Levels of FT_4 and hCG were significantly higher in the women with hyperemesis, but hCG levels correlated significantly and positively with FT_4 levels and negatively with TSH levels only in the hyperemesis group. Other studies have replicated these results and shown suppression of TSH when compared with controls (37). Hyperemesis gravidarum is associated with

biochemical hyperthyroidism but rarely with clinical hyperthyroidism and is largely transitory, requiring no treatment. Routine measurements of thyroid function are not recommended in patients with hyperemesis gravidarum unless other overt signs of hyperthyroidism are evident.

How is thyroid storm diagnosed and treated in pregnancy?

Thyroid storm is a medical emergency characterized by an extreme hypermetabolic state. It is rare—occurring in 1% of pregnant patients with hyperthyroidism—but has a high risk of maternal heart failure (9). Older literature described a maternal mortality of up to 25% but this has not been substantiated by more recent data (9, 41). Thyroid storm is diagnosed by a combination of the following signs and symptoms: fever; tachycardia out of proportion to the fever; changed mental status, including restlessness, nervousness, confusion, and seizures; vomiting; diarrhea; and cardiac arrhythmia (42). Often there is an identified inciting event such as infection, surgery, labor, or delivery. However, the diagnosis can be difficult to make and requires expedient treatment to avoid the severe consequences of untreated thyroid storm, which include shock, stupor, and coma. If thyroid storm is suspected, serum FT_4, FT_3, and TSH levels should be evaluated to help confirm the diagnosis, but therapy should not be withheld pending the results.

Therapy for thyroid storm consists of a standard series of drugs (see box) (8, 42). Each drug has a specific role in the suppression of thyroid function. Propylthiouracil or methimazole blocks additional synthesis of thyroid hormone, and PTU also inhibits peripheral conversion of T_4 to T_3. Saturated solution of potassium iodide and sodium iodide block the release of thyroid hormone from the gland. Dexamethasone decreases thyroid hormone release and peripheral conversion of T_4 to T_3, and propranolol inhibits the adrenergic effects of excessive thyroid hormone. Finally, phenobarbital can be used to reduce extreme agitation or restlessness and may increase the catabolism of thyroid hormone (42). In addition to pharmacologic management, general supportive measures should be undertaken, including administration of oxygen, maintenance of intravascular volume and electrolytes, use of antipyretics, use of a cooling blanket, and appropriate maternal and fetal monitoring; invasive central monitoring and continuous maternal cardiac monitoring in an intensive care setting may be indicated. Coincident with treating the thyroid storm, the perceived underlying cause of the storm should be treated. As with other acute maternal illnesses, fetal well-being should be appropriately evaluated with ultrasonography, biophysical profile, or nonstress test depending on the gestational age of the fetus. In general, it is prudent to avoid delivery in the presence of thyroid storm unless fetal indications for delivery outweigh the risks to the woman.

Treatment of Thyroid Storm in Pregnant Women

1. Propylthiouracil (PTU), 600–800 mg orally, stat, then 150–200 mg orally every 4–6 hours. If oral administration is not possible, use methimazole rectal suppositories.
2. Starting 1–2 hours after PTU administration, saturated solution of potassium iodide (SSKI), 2–5 drops orally every 8 hours, *or*

   sodium iodide, 0.5–1.0 g intravenously every 8 hours, *or*

   Lugol's solution, 8 drops every 6 hours, *or*

   lithium carbonate, 300 mg orally every 6 hours.
3. Dexamethasone, 2 mg intravenously or intramuscularly every 6 hours for four doses.
4. Propranolol, 20–80 mg orally every 4–6 hours, *or* propranolol, 1–2 mg intravenously every 5 minutes for a total of 6 mg, then 1–10 mg intravenously every 4 hours.

   If the patient has a history of severe bronchospasm:

   Reserpine, 1–5 mg intramuscularly every 4–6 hours

   Guanethidine, 1mg/kg orally every 12 hours

   Diltiazem, 60 mg orally every 6–8 hours
5. Phenobarbital, 30–60 mg orally every 6–8 hours as needed for extreme restlessness.

Data from Ecker JL, Musci TJ. Thyroid function and disease in pregnancy. Curr Probl Obstet Gynecol Fertil 2000;23:109–122; and Molitch ME. Endocrine emergencies in pregnancy. Bailliere's Clin Endocrinol Metab 1992;6:167–191

How should a thyroid nodule or thyroid cancer during pregnancy be assessed?

The incidence of thyroid cancer in pregnancy is 1 per 1,000 (43). Any thyroid nodule discovered during pregnancy should be diagnostically evaluated, because malignancy will be found in up to 40% of these nodules (34, 44). Pregnancy itself does not appear to alter the course of thyroid cancer (43, 45). Whether pregnancy increases the risk of recurrence of thyroid cancer or the risk that a thyroid nodule becomes cancerous is less clear

(34). In a cohort study comparing thyroid cancer in pregnant or postpartum women with nonpregnant women, there were no differences in the presenting physical findings, tumor type, tumor size, presence of metastases, time between diagnosis and treatment, recurrence rates, or death rates (43). Women in this study were monitored for a median of 20 years. These data strongly suggest that pregnancy does not affect the outcome of thyroid cancer. In addition, except for the time between diagnosis and surgery, there was no difference in outcome between those women who had thyroidectomy during pregnancy and those who had the procedure after pregnancy. Significantly more pregnant women had no symptoms, emphasizing the importance of the physical examination during pregnancy.

Another study compared pregnancy outcomes among women with thyroid cancer who fell into 1 of 3 categories: 1) before treatment, 2) after thyroidectomy but before I-131 treatment, and 3) after treatment with both thyroidectomy and I-131 (46). The study found no differences in stillbirths, LBW, or malformations among the three groups. The incidence of spontaneous abortion was significantly higher in women who had any treatment for thyroid cancer but was not different between those women who had surgery only and those who had surgery and I-131 treatment.

If a diagnosis of cancer is made, a multidisciplinary treatment plan should be determined. The options are pregnancy termination, treatment during pregnancy, and preterm or term delivery with treatment after pregnancy. This decision will be affected by the gestational age at diagnosis and the tumor characteristics. Definitive treatment for thyroid cancer is thyroidectomy and radiation. Thyroidectomy can be performed during pregnancy, preferably in the second trimester, but radiation should be deferred until after pregnancy. Breastfeeding should be avoided for at least 120 days after I-131 treatment (34).

▶ *How is postpartum thyroiditis diagnosed and treated?*

Postpartum thyroiditis occurs in 5% of women who do not have a history of thyroid disease (47). Studies have found that approximately 44% of women with postpartum thyroiditis have hypothyroidism, while the remaining women are evenly split between thyrotoxicosis and thyrotoxicosis followed by hypothyroidism (47, 48). In one study, goiter was present in 51% of women with postpartum thyroiditis (48). Postpartum thyroiditis also may occur after pregnancy loss and has a 70% risk of recurrence (49, 50).

The diagnosis of postpartum thyroiditis is made by documenting new-onset abnormal levels of TSH or FT_4 or both. If the diagnosis is in doubt, measuring antimicrosomal or thyroperoxidase antithyroid peroxidase antibodies may be useful to confirm the diagnosis.

The need for treatment in women with postpartum thyroiditis is less clear. In a prospective study of 605 asymptomatic pregnant and postpartum women, only five women, or 11% of the women diagnosed with postpartum thyroiditis, developed permanent hypothyroidism (48). Furthermore, none of the women with thyrotoxicosis required treatment, and only 40% of those with hypothyroidism required treatment (48). Those who were treated received T_4 for extremely high levels of TSH with suppressed T_4 or increasing goiter size. Because of the low incidence of postpartum thyroiditis and the low likelihood of requiring treatment, screening with TFTs and antimicrosomal antibodies in asymptomatic women is not warranted (47, 51).

Women who develop a goiter in pregnancy or postpartum or who develop postpartum hypothyroid or hyperthyroid symptoms (including excessive fatigue, weight gain, dry skin, dry hair, cold intolerance, persistent amenorrhea, difficulty concentrating, depression, nervousness, or palpitations) should have their TSH and FT_4 levels evaluated (47, 48, 51). As noted previously, thyroid antimicrosomal or antithyroid peroxidase antibodies also may be useful. Because some of these symptoms are common in the postpartum state, clinicians must use their judgment to determine whether the symptoms warrant evaluation. If the patient has hypothyroidism, the decision to treat depends on the severity of abnormality and symptoms. Women with the highest levels of TSH and antithyroid peroxidase antibodies have the highest risk for developing permanent hypothyroidism (48).

▶ *Which pregnant patients should be screened for thyroid dysfunction?*

It is appropriate to perform indicated testing of thyroid function in women with a personal history of thyroid disease or symptoms of thyroid disease. The performance of TFTs in asymptomatic pregnant women who have a mildly enlarged thyroid is not warranted. Development of a significant goiter or distinct nodules should be evaluated as in any patient.

An observational study has drawn considerable attention to the subject of maternal subclinical hypothyroidism and resulted in calls from some professional organizations for universal screening for maternal hypothyroidism (20). Investigators screened maternal serum samples—obtained in the second trimester for purposes of maternal serum alphafetoprotein screening for neural tube defects—for elevated TSH levels (20). Out of 25,216 samples, only 75 women had TSH levels above the 99.7th percentile. The investigators then compared the results of neuropsycho-

logic testing for 62 children of hypothyroid women with those of 124 children of matched women with normal thyroid glands when the children were approximately 8 years of age. They found no significant difference in mean IQ scores between the children of hypothyroid women and controls ($P = 0.06$). There was a significant difference in mean IQ scores when the children of untreated hypothyroid women were compared with controls but not between children of untreated and treated hypothyroid women. Among the children of the untreated women, 19% had full-scale IQ scores of 85 or lower, compared with only 5% of the children of women with normal thyroid glands.

It is important to acknowledge the limitations of the current understanding of this issue. The data available are observational. There have been no intervention trials to demonstrate the efficacy of screening and treatment to improve neuropsychologic performance in the offspring of hypothyroid women. The available data are consistent with the possibility that maternal hypothyroidism is associated with a decrement in some neuropsychologic testing. However, the association needs further testing to document its validity and, if confirmed, evidence that treatment ameliorates the effect. For all of these reasons, it would be premature to recommend universal screening for hypothyroidism during pregnancy.

Summary of Recommendations

The following recommendation is based on good and consistent scientific evidence (Level A):

- Levels of TSH or FT_4/FTI should be monitored to manage thyroid disease in pregnancy.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- Either PTU or methimazole can be used to treat pregnant women with hyperthyroidism.
- Thyroid function tests are not indicated in asymptomatic pregnant women with slightly enlarged thyroid glands.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- There is no need to measure TFTs routinely in women with hyperemesis.
- There are insufficient data to warrant routine screening of asymptomatic pregnant women for hypothyroidism.
- Indicated testing of thyroid function may be performed in women with a personal history of thyroid disease or symptoms of thyroid disease.
- The presence of maternal thyroid disease is important information for the pediatrician to have at the time of delivery.
- Thyroid nodules should be investigated to rule out malignancy.

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The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and August 2000. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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