Hypothyroidism during pregnancy: Clinical manifestations, diagnosis, and treatment

Author: Douglas S Ross, MD
Section Editors: David S Cooper, MD, Charles J Lockwood, MD, MHCM
Deputy Editor: Jean E Mulder, MD

All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: May 2017. | **This topic last updated:** Apr 14, 2017.

INTRODUCTION — The evaluation and treatment of pregnant women with hypothyroidism parallels that of nonpregnant women and men but presents some unique problems. There are several important issues that must be considered when hypothyroidism occurs during pregnancy or when women with preexisting treated hypothyroidism become pregnant. The clinical manifestations, diagnosis, and treatment of hypothyroidism during pregnancy are reviewed here. Other aspects of thyroid disease during pregnancy are reviewed elsewhere:

- (See "Overview of thyroid disease in pregnancy".)
- (See "Hyperthyroidism during pregnancy: Clinical manifestations, diagnosis, and causes".)
- (See "Hyperthyroidism during pregnancy: Treatment".)

CLINICAL FEATURES

Clinical manifestations — The range of clinical symptoms of hypothyroidism during pregnancy is similar to those that occur in nonpregnant patients and may include fatigue, cold intolerance, constipation, and weight gain. Symptoms may be overlooked or attributed to the pregnancy itself as some of the symptoms of hypothyroidism are similar to those of pregnancy (although cold intolerance is not a normal clinical manifestation of pregnancy). Many patients are asymptomatic. (See "Clinical manifestations of hypothyroidism".)

Laboratory findings — To meet the increased metabolic needs during a normal pregnancy, there are changes in thyroid physiology that are reflected in altered thyroid function tests. These changes include an increase in thyroxine (T4)-binding globulin (TBG), which results in total T4 and triiodothyronine (T3) concentrations that are higher than in nonpregnant women. In addition, high serum human chorionic gonadotropin (hCG) levels, particularly during early pregnancy, result in a reduction in first trimester serum thyroid-stimulating hormone (TSH) concentrations. (See "Overview of thyroid disease in pregnancy", section on 'Thyroid adaptation during normal pregnancy'.)

Because of the changes in thyroid physiology during normal pregnancy and because there are substantial population differences in the TSH upper reference limit, thyroid function tests should be interpreted using population-based, trimester-specific reference ranges for TSH and assay method and trimester-specific reference ranges for serum free T4. (See "Overview of thyroid disease in pregnancy", section on 'Trimester-specific reference ranges'.)

- If the laboratory does not provide population and trimester-specific reference ranges for TSH, an upper reference limit of approximately 4.0 mU/L can be used.
- Trimester-specific reference ranges for free T4 should be provided with the assay kits. If not available (and particularly if free T4 values are discordant from serum TSH), measurement of total T4 may be superior to free T4 in the second and third trimesters. Total T4 levels during later pregnancy are approximately 1.5-fold higher than in nonpregnant women.

Thyroid peroxidase (TPO) antibodies are elevated in 30 to 60 percent of pregnant women with an elevated TSH [1,2]. Women who have subclinical hypothyroidism with positive TPO antibodies have a higher risk of pregnancy complications than those whose TPO antibodies are negative [3]. (See 'Subclinical hypothyroidism' below.)

DIAGNOSIS — The diagnosis of primary hypothyroidism during pregnancy is based upon the finding of an elevated serum TSH concentration, defined using population and trimester-specific TSH reference ranges for pregnant women [4]. (See "Overview of thyroid disease in pregnancy", section on 'Trimester-specific reference ranges'.)

TSH should be measured in any women with symptoms of hypothyroidism. Screening of asymptomatic women is reviewed below. (See 'Screening' below.)

For women in the first trimester of pregnancy with a TSH above the population and trimester-specific upper limit of normal or above 4.0 mU/L when local reference ranges are not available, we also measure a free T4 (or total T4, if trimester-specific reference range for free T4 is not provided or if free T4 measurements appear discordant with TSH measurements). In addition, we agree with the American Thyroid Association (ATA) recommendation to measure thyroid peroxidase (TPO) antibodies in pregnant women with TSH >2.5 mU/L to inform treatment considerations [4]. (See 'Indications for treatment' below.)

- Overt primary hypothyroidism is defined as an elevated trimester-specific TSH concentration in conjunction with a decreased free T4 concentration (below assay normal using reference range for pregnant women).
- Subclinical hypothyroidism is defined as an elevated trimester-specific serum TSH concentration and a normal free T4 concentration.

Women with central hypothyroidism from pituitary or hypothalamic disease will not have elevated TSH concentrations during pregnancy. (See "Central hypothyroidism", section on 'Diagnosis'.)

PREGNANCY COMPLICATIONS — Hypothyroidism can have adverse effects on pregnancy outcomes, depending upon the severity of the biochemical abnormalities:

- Overt hypothyroidism
- Subclinical hypothyroidism
- Maternal hypothyroxinemia (isolated low maternal free T4)

Overt hypothyroidism — Overt hypothyroidism (elevated TSH, reduced free T4) complicating pregnancy is unusual (0.3 to 0.5 percent of screened women). Two factors contribute to this finding; some hypothyroid women are anovulatory [5], and hypothyroidism (new or inadequately treated) complicating pregnancy is associated with an increased rate of first trimester spontaneous abortion [6-8].

In continuing pregnancies, hypothyroidism has been associated with an increased risk of several complications, including [9-18]:

- Preeclampsia and gestational hypertension
- Placental abruption
- Nonreassuring fetal heart rate tracing
- Preterm delivery, including very preterm delivery (before 32 weeks)
- Low birth weight (which was likely due to preterm delivery for preeclampsia in one study [13] but not in a second study where the rate of preeclampsia was negligible [17])
- Increased rate of cesarean section
- Postpartum hemorrhage
- Perinatal morbidity and mortality
- Neuropsychological and cognitive impairment in the child

Subclinical hypothyroidism — Subclinical hypothyroidism (elevated TSH, normal free T4) is more common than overt hypothyroidism, occurring in 2.0 to 2.5 percent of screened women in the United States (iodine-sufficient region) [1,19].

Adverse pregnancy outcome — The risk of complications during pregnancy is lower in women with subclinical, rather than overt, hypothyroidism. However, in some [3,13,20-25], but not all [26], studies, women with subclinical hypothyroidism were also reported to be at increased risk for severe preeclampsia, preterm delivery, placental abruption, and/or pregnancy loss compared with euthyroid women.

In a systematic review and meta-analysis of 18 cohort studies, pregnant women with subclinical hypothyroidism were at higher risk for placental abruption (relative risk [RR] 2.14), pregnancy loss (RR 2.01), premature rupture of membranes (RR 1.43), and neonatal death (RR 2.58) compared with euthyroid women [27]. The risks of preterm delivery and preeclampsia did not reach or were of borderline statistical significance, respectively (RRs 1.20, 95% CI 0.97-1.50 and 1.30, 95% CI 1.00-1.68). Limitations of the analysis included variability among the studies in the upper reference limit of TSH used to define subclinical hypothyroidism and inconsistent accounting for thyroid antibody status.

Assessment of antibody status is important because women with subclinical hypothyroidism and positive anti-thyroid peroxidase (TPO) antibodies tend to have the highest risk of adverse pregnancy outcomes, and adverse outcomes occur at a lower TSH than in women without TPO antibodies [3]. In the American Thyroid Association (ATA) systematic review (ATA guidelines on thyroid disease during pregnancy), the risk of pregnancy-specific complications was apparent in TPO-positive women with TSH >2.5 mU/L but was not consistently apparent in TPO-negative women until TSH values exceeded 5 to 10 mU/L [4]. (See "Overview of thyroid disease in pregnancy", section on 'Thyroid peroxidase antibodies in euthyroid women'.)

In addition, limited data suggest that pregnancy outcome for women undergoing in vitro fertilization may be worse among those with preconception TSH levels higher than 2.5 mU/L. As an example, in one study of delivery outcomes after in vitro fertilization, gestational age and birth weight were higher for 150 deliveries where preconception TSH was <2.5 mU/L compared with 45 deliveries where TSH was >2.5 mU/L [28].

Cognitive impairment — It is uncertain if the children of women with subclinical hypothyroidism are at risk for neuropsychological impairment. Observational studies suggest an association between subclinical hypothyroidism in pregnancy and impaired cognitive development in children [15,29-31].

In one report of seven- to nine-year-old children, the mean intelligence quotient (IQ) score at age five years was slightly lower in 62 children whose mothers had high serum TSH concentrations (above 98th percentile for pregnancy, mean 13.2 mU/L) during the second trimester than in 124 children of mothers who had normal serum TSH concentrations (103 versus 107, p = 0.06) [15]; 15 percent of the former had a score of 85 or lower, as compared with 5 percent of the latter. Some experts speculate that preterm delivery may explain some of the neurocognitive dysfunction (when found) in the children of women with subclinical hypothyroidism [20]. However, an analysis of maternal thyroid function at delivery of preterm infants (born ≤34 weeks) and neurodevelopmental outcome assessed at 5.5 years of age demonstrated significant decrements in general cognition and verbal and perceptual performance subscales for each mU/L increment in maternal TSH [32].

In another report, 54 children born to mothers with mean TSH 7.81 mU/L in the first trimester (all treated with levothyroxine) had smaller hippocampal volume and lower scores on memory testing, suggesting either no effect of levothyroxine or that the levothyroxine was not initiated sufficiently early [18].

Effect of thyroid hormone replacement — It is uncertain if thyroid hormone replacement reduces the risk of adverse pregnancy, neonatal, and/or childhood cognitive outcomes in women with subclinical hypothyroidism. The limitations of the existing trial data include initiation of levothyroxine after the first trimester, which may be too late, and the mild degree of TSH elevation in the mothers participating in the studies.

- **Pregnancy outcomes** – Studies assessing the benefit of levothyroxine therapy in reducing adverse pregnancy outcomes show conflicting results [33-36]. As examples:

  - In a trial of 131 women with positive TPO antibodies (euthyroidism or subclinical hypothyroidism) randomly assigned to treatment with levothyroxine or no treatment, treatment with levothyroxine significantly decreased the rate of preterm delivery, particularly in women with TSH ≥4 mU/L (5.3 versus 29.4 percent in control group) [33].

  - In a randomized trial that was designed to assess a case-finding versus a universal thyroid screening strategy, over 4500 women in their first trimester of pregnancy were randomly assigned to universal screening or case-finding groups (see 'Screening' below) [35]. All patients in the universal screening group and all high-risk patients in the case-finding group were tested for free T4, TSH, and TPO antibody levels in the first trimester, and those with positive TPO antibody titers were treated if the serum TSH was greater than 2.5 mU/L. Low-risk women in the case-finding group had their first trimester blood samples assayed postpartum. Overall, there was no significant difference in the total number of adverse outcomes between the case-finding and universal screening groups.

    However, in a secondary analysis, low-risk women in the universal screening group who were found to have subclinical hypothyroidism (TSH greater than 2.5 mU/L and positive antibody titers) and were treated with thyroid hormone had fewer adverse outcomes (miscarriage, hypertension, preeclampsia, gestational diabetes, preterm labor, preterm delivery, and many others) than the low-risk patients in the case-finding group with subclinical hypothyroidism who were not treated (odds ratio [OR] 0.43, 95% CI 0.26-0.70) [35].

  - In a multicenter trial, 677 pregnant women (mean 16.6 weeks gestation) with subclinical hypothyroidism (median TSH 4.4 mU/L with normal free T4) were randomly assigned to levothyroxine or placebo [36]. There were no significant differences in the frequencies of preterm delivery, preeclampsia, gestational hypertension, miscarriage rate, or other maternal or fetal outcomes. There was no interaction according to TPO antibody positivity.

- **Cognitive development** – There are insufficient data to determine whether there is an effect of maternal levothyroxine treatment on neurocognitive outcomes in the children of mothers with subclinical hypothyroidism. The limitations of the existing data include initiation of levothyroxine after the first trimester, which may be too late, and the mild degree of TSH elevation in the mothers participating in the studies. As examples:

  - In a randomized trial comparing screening for and treatment of thyroid dysfunction in early pregnancy with a control group (serum samples from the control group were stored and assayed after delivery), there were no differences between the two groups in the neurocognitive outcomes of the children [34]. Specifically, in the mothers who had tested positive for thyroid dysfunction (TSH >3.65 mU/L, serum free T4 below the 2.5th percentile, or both), approximately half of whom received levothyroxine, there were no differences in:

    - The IQ of the children at three years of age (100 versus 99.2)
    - The proportion of children with IQ score <85 (12.1 and 14.1 percent in the screening and control groups, respectively)

    The mean serum TSH was 3.8 mU/L (compared with 13.2 mU/L in one observational study [15]), and treatment was initiated at a median gestational age of 13 weeks. Approximately 25 percent of children in each group did not complete psychological testing. It is uncertain if treatment earlier in gestation or testing of children at an older age would change the outcome. It is also possible that the study population included women with very mild subclinical hypothyroidism, where an effect on cognitive development would be less likely to have been observed.

- In a multicenter trial, 677 pregnant women (mean 16.6 weeks gestation) with subclinical hypothyroidism (median TSH 4.4 mU/L, normal free T4) were randomly assigned to levothyroxine or placebo [36]. There were no significant differences in neurodevelopmental (median IQ scores 97 and 94, respectively) or behavioral outcomes in the children at five years of age. There was no interaction according to TPO antibody positivity.

Although existing evidence argues against neurocognitive benefit associated with treating subclinical hypothyroidism in pregnancy, additional randomized trials are needed to determine whether earlier initiation of treatment (prior to 13 weeks) improves outcomes.

Low maternal free T4 — Isolated maternal hypothyroxinemia (low T4) is defined as a maternal free T4 concentration in the lower 2.5th to 5th percentile of the reference range, in conjunction with a normal TSH. The effect of isolated maternal hypothyroxinemia on perinatal and neonatal outcome is unclear [2,14,26,29,37,38].

- **Pregnancy outcomes** – In one study, maternal serum free T4 concentrations below the 2.5th percentile (with normal TSH) were not associated with adverse pregnancy outcomes [2]. However, in the First and Second Trimester Evaluation of Risk (FASTER) consortium, among the women with hypothyroxinemia and normal TSH (232 and 247 women in the first and second trimesters, respectively), there was an increased OR for preterm labor (1.62, 95% CI 1.00-2.62), macrosomia (1.97, 95% CI 1.37-2.83), and gestational diabetes (1.70, 95% CI 1.02-2.84) [26]. In the Generation R study, maternal hypothyroxinemia was associated with a 2.5-fold increased risk of premature delivery [23].

- **Cognitive outcomes** – In some studies, infants and toddlers whose mothers had reduced serum free T4 concentrations (with normal TSH) during gestation (12 to 20 weeks) had lower mean intelligence, psychomotor, or behavioral scores compared with children born to women with normal thyroid function during gestation [14,29,37-39]. As an example, in one study of 3727 mother-child pairs, the children of mothers whose free T4 was in the lowest 5 percent during the first trimester had IQ scores at six years of age that were 4.3 points lower than the children of mothers with higher free T4 concentrations [40]. Other studies have shown an increased frequency of autism and attention deficit disorder in offspring of hypothyroxinemic women [41,42].

  In contrast, a case-control study that examined children at age two years born to mothers who had second trimester free T4 levels <3rd centile versus those with free T4 levels between the 10th and 90th centile did not find any differences in neurocognitive development [43].

- **Effect of thyroid hormone replacement** – In two randomized trials, there was no difference in the IQ of children of mothers with low free T4 who did or did not receive T4 treatment at a median gestational age of 13 or 16 weeks [34,36]. As an example, in a multicenter trial, 526 pregnant women (mean 17.8 weeks gestation) with isolated maternal hypothyroxinemia (median free T4 0.83 ng/dL with normal TSH [median 1.5 mU/L]) were randomly assigned to levothyroxine or placebo [36]. There were no significant differences in neurodevelopmental (median IQ scores 94 and 91, respectively) or behavioral outcomes in the children at five years of age. In addition, there were no significant differences in the frequencies of preterm delivery, preeclampsia, gestational hypertension, miscarriage rate, or other maternal or fetal outcomes.

SCREENING — Because overt and subclinical hypothyroidism are associated with pregnancy complications, including pregnancy loss, and thyroid tests are widely available and easy to perform, there is interest in screening for thyroid dysfunction in asymptomatic pregnant women. The universal screening of asymptomatic pregnant women for thyroid dysfunction during the first trimester of pregnancy is controversial, however, because of insufficient data showing a benefit of thyroid hormone replacement. Thus, there is wide variation in screening practices [44-47].

Whom to screen — Because of insufficient evidence to support universal TSH screening in the first trimester, we and others [4,48,49] prefer a targeted approach to screening (ie, "case finding"). Pregnant women with any of the following are candidates for screening:

- Living in an area of moderate to severe iodine insufficiency
- Symptoms of hypothyroidism
- Family or personal history of thyroid disease
- Personal history of:
  - Thyroid peroxidase (TPO) antibodies
  - Goiter
  - Age >30 years
  - Type 1 diabetes
  - Head and neck irradiation
  - Recurrent miscarriage or preterm delivery
  - Multiple prior pregnancies (two or more)
  - Morbid obesity (body mass index [BMI] ≥40 kg/m^2)
  - Infertility

- Prior thyroid surgery
- Use of amiodarone, lithium, or recent administration of iodinated radiologic contrast agents

The results of observational studies suggest that assessment of thyroid function only in women at high risk for thyroid or other autoimmune disease (targeted screening) will miss up to one-third of women with subclinical or overt hypothyroidism (TSH >3.5 to 4.2 mU/L) [46,50,51]. However, in prospective trials, universal screening compared with a targeted approach or with no screening did not improve pregnancy outcomes [34,35].

As an example, in the trial described above (over 4500 women in their first trimester of pregnancy randomly assigned to universal screening or case-finding groups, and those with positive TPO antibody titers were treated if the serum TSH was greater than 2.5 mU/L), there were no significant differences in adverse outcomes between the case-finding and universal screening groups [35]. The majority of the women in the low-risk case-finding group were euthyroid (97.9 percent), whereas hypothyroidism was found in 34 (1.9 percent) and hyperthyroidism in five (0.2 percent) women. Because these samples were assayed postpartum, these women were not treated. The case-finding approach missed 34 of 54 hypothyroid women. (See 'Effect of thyroid hormone replacement' above.)

In another randomized trial, antenatal screening (median gestational age 12 weeks) and maternal treatment of subclinical hypothyroidism at a mean of 13 weeks did not result in improved pregnancy-related outcomes or cognitive function in children at three years of age compared with controls in whom blood was drawn and stored for testing after delivery [34]. (See 'Effect of thyroid hormone replacement' above.)

Limited data suggest that universal screening may be more cost effective than not screening [52,53]. One analysis found that universal screening compared with risk-based screening resulted in an incremental cost-effectiveness ratio of USD $7258 per quality-adjusted life-year [53].

Approach to screening — In women who meet the case-finding criteria, we suggest measurement of serum TSH during the first trimester as the screening test for hypothyroidism:

- If the serum TSH is between the trimester-specific lower limit of normal and 2.5 mU/L, most women require no further testing.

  However, in women at particularly high risk for developing hypothyroidism during pregnancy (TPO antibody positive, post-radioiodine treatment, post-hemithyroidectomy, history of childhood exposure to high-dose irradiation of the head or neck region), we reassess TSH during pregnancy (eg, approximately every four weeks during the first trimester, and then once during each of the second and third trimesters).

- If the serum TSH is >2.5 mU/L, we measure TPO antibodies.

  The presence of TPO antibodies may be useful for making treatment decisions in women with borderline thyroid function tests (eg, TSH 2.5 to 4.0 mU/L) and in predicting the development of hypothyroidism and the risk of miscarriage and postpartum thyroid dysfunction. (See 'Indications for treatment' below and "Postpartum thyroiditis".)

- If the TSH is >4 mU/L, we suggest measurement of free T4 to determine the degree of hypothyroidism.

TREATMENT — Our approach to treatment outlined below is largely consistent with the Guidelines of the American Thyroid Association (ATA) and the Endocrine Society for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum [4,49].

Indications for treatment

- **TSH >4 mU/L** – All pregnant women with newly diagnosed, overt hypothyroidism (TSH above trimester-specific normal reference range [or above 4.0 mU/L if trimester-specific range unavailable] with low free T4) should be treated with thyroid hormone (levothyroxine, T4). (See 'Levothyroxine initial dosing' below.)

  Because maternal euthyroidism is potentially important for normal fetal cognitive development, we and others [49] suggest treatment of pregnant women with subclinical hypothyroidism (TSH above trimester-specific normal reference range [or above 4.0 mU/L if trimester-specific range unavailable], with normal free T4), regardless of thyroid peroxidase (TPO) antibody status (see 'Subclinical hypothyroidism' above). This approach differs slightly from the ATA guidelines (reviewed at the end of this section), in which treatment recommendations are based on TPO antibody status [4].

- **TSH 2.6 to 4 mU/L** – For pregnant women with a TSH between 2.6 and 4 mU/L, positive TPO antibodies, and history of recurrent miscarriage, we suggest treatment with T4.

  For pregnant women with TSH in this range and no prior history of miscarriage, we individualize the decision to treat based upon the presence of TPO antibodies and patient values and preferences. The data assessing treatment with T4 in this subgroup of women are conflicting and limited by variability in the TSH criteria used to define hypothyroidism and the late initiation of thyroid hormone treatment (often late in the first trimester). (See 'Subclinical hypothyroidism' above.)

Some UpToDate editors and the author of this topic review offer T4 treatment (50 mcg daily) in TPO-positive women with TSH >2.5 mU/L. Others treat pregnant women with TPO antibodies, regardless of the TSH level, while others do not routinely treat euthyroid, TPO-positive women with T4, because of insufficient evidence of benefit.

In pregnant women with TSH between 2.6 and 4 mU/L who are not treated with thyroid hormone, TSH should be reassessed during pregnancy (eg, approximately every four weeks during the first trimester and once during each of the second and third trimesters for TPO-positive women, and at least once more during the first trimester and again mid-pregnancy for TPO-negative women). If TSH rises above the population and trimester-specific upper limit of normal (approximately 4 mU/L), we begin treatment with T4.

- **TSH between the trimester-specific lower limit of normal and 2.5 mU/L** – These women are euthyroid and do not require T4 treatment. However, if there is a prior history of recurrent miscarriage, TPO antibodies have typically already been assessed, and thyroid hormone treatment (T4, 50 mcg daily) offered to TPO antibody-positive patients. The management of women with TPO antibodies and normal thyroid function is reviewed elsewhere. (See "Overview of thyroid disease in pregnancy", section on 'Thyroid peroxidase antibodies in euthyroid women' and "Management of couples with recurrent pregnancy loss", section on 'Thyroid dysfunction and diabetes mellitus'.)

- **Low free T4, normal TSH (maternal hypothyroxinemia)** – We do not typically treat pregnant women with isolated hypothyroxinemia (low free T4, normal TSH). (See 'Low maternal free T4' above.)

The ATA guidelines base their treatment recommendations on TPO antibody status [4]. They recommend measurement of TPO antibodies in pregnant women with TSH >2.5 mU/L and treatment as follows:

- Positive TPO antibodies: Thyroid hormone should be considered if TSH is above 2.5 mU/L and should be initiated if TSH is above the population and trimester-specific upper limit of normal (approximately 4.0 mU/L).

- Negative TPO antibodies: Thyroid hormone should be considered if the TSH is above population and trimester-specific upper limit of normal but <10 mU/L and should be initiated if the TSH is >10 mU/L.

- Maternal hypothyroxinemia: The ATA does not suggest treatment of pregnant women with isolated hypothyroxinemia (low free T4, normal TSH).

Newly diagnosed hypothyroidism

Levothyroxine initial dosing — The treatment of choice for correction of hypothyroidism in pregnancy is the same as in nonpregnant patients: synthetic levothyroxine (T4). Several formulations of T4 are available. Because there may be subtle differences in bioavailability between T4 formulations, some endocrinologists feel that it is preferable to stay with the same formulation whenever possible. When using generic preparations, the manufacturer can be identified from the prescription label, and the patient may request refills from the same generic pharmaceutical company.

The goal of T4 replacement in pregnancy is to restore euthyroidism as soon as possible. General dosing guidance is as follows:

- TSH >4 mU/L (or above population and trimester-specific upper limit of normal), with low free T4 (using assay method and trimester-specific reference range): Close to full replacement dose (approximately 1.6 mcg/kg body weight per day)

- TSH >4 mU/L, with normal free T4: Intermediate dose (approximately 1 mcg/kg per day)

- TSH 2.6 to 4 mU/L: If a decision has been made to treat, low dose (typically 50 mcg daily)

T4 should be taken on an empty stomach, ideally an hour before breakfast, but few patients are able to wait a full hour.

Monitoring and dose adjustments — After initiation of T4 therapy, the patient should be reevaluated and serum TSH measured in four weeks.

The goal is to maintain TSH in the lower half of the trimester-specific reference range. If not available, a goal TSH of <2.5 mU/L is reasonable.

If the TSH remains above the normal trimester-specific reference range, the dose of T4 can be increased by 12 to 25 mcg/day. TSH should be measured every four weeks during the first half of pregnancy because dose adjustments are often required. TSH can be monitored less often (at least once each trimester) in the latter half of pregnancy, as long as the dose is unchanged.

Postpregnancy adjustments — Since the criteria for treating pregnant women differ from the criteria from treating nonpregnant women, it is not always necessary to continue levothyroxine after delivery. In one study, 75 percent of women with subclinical hypothyroidism during pregnancy had normal thyroid function five years postpartum [54]. Because overt hypothyroidism may interfere with milk production, it may be prudent to delay assessment until the completion of breastfeeding. Unless another pregnancy is imminent, however, the majority of women who were started on levothyroxine for TSH between 2.5 and 4.0 mU/L do not need to continue levothyroxine treatment.

Preexisting hypothyroidism

Goal preconception TSH — Women with preexisting hypothyroidism who are planning to become pregnant should optimize their thyroid hormone dose preconception. The goal preconception serum TSH level is between the lower reference limit and 2.5 mU/L [4,49]. However, some experts prefer a lower preconception TSH level (<1.2 mU/L).

Approximately 50 to 85 percent of women with preexisting hypothyroidism need more T4 during pregnancy [6,55-57]. In one study, only 17 percent of women with preconception TSH values <1.2 mU/L required a dose increase during the subsequent pregnancy, compared with 50 percent of women with preconception TSH levels between 1.2 and 2.4 mU/L [58]. Preconception counseling is important in this regard. Studies have shown that approximately 30 percent of women taking levothyroxine have a serum TSH >4 mU/L when they present for their first prenatal visit [59]. In such women, serum TSH of 4.5 to 10 compared with <2.5 mU/L at the time of presentation is a predictor of miscarriage (odds ratio [OR] 1.80, 95% CI 1.03-3.14) [60]. The risk of miscarriage was even higher in women with TSH >10 mU/L at presentation (OR 3.95, 95% CI 1.87-8.37).

Early dose adjustments — Given that T4 dose requirements may increase during pregnancy in women with preexisting hypothyroidism, hypothyroid women who are newly pregnant should **preemptively** increase their levothyroxine dose by approximately 30 percent and notify their clinician promptly. We typically accomplish this by increasing the dose from once-daily dosing to a total of nine doses per week (double the daily dose two days each week). Further dose changes are made based upon serum TSH concentrations measured every four weeks until the TSH becomes normal. Using such an approach, only 2 of 25 women in one randomized trial had TSH values greater than 5 mU/L during pregnancy, although eight women had TSH values greater than 2.5 mU/L during the first trimester or greater than 3.0 mU/L during the second or third trimesters, and two had TSH values <0.1 mU/L [61].

Another approach is to measure serum TSH as soon as pregnancy is confirmed, then again four weeks later, four weeks after any change in the dose of T4, and at least once each trimester [55]. The dose should be adjusted as needed every four weeks to achieve a normal TSH level. (See "Treatment of primary hypothyroidism in adults", section on 'Initial monitoring and dose adjustments'.)

Dose requirements may increase by as much as 50 percent during pregnancy, and the increase occurs as early as the fifth week of gestation as illustrated by the following:

- In a prospective study of 20 pregnancies in 19 hypothyroid women in whom serum TSH was measured every two weeks in the first trimester and then every four weeks thereafter, a T4 dose increase (on average by 47 percent) was necessary in 17 of the 20 pregnancies [56]. Although the median onset of the dose modification occurred at eight weeks with a plateau at 16 weeks of gestation, some women required an increase in dose as early as the fifth week. The higher dose was required until delivery.
- In a retrospective, population-based analysis of 950 pregnancies in hypothyroid women, 60 percent required a levothyroxine dose increase (34 percent during the first trimester) [57].

Unlike normal women, those with preexisting hypothyroidism or subclinical hypothyroidism are unable to increase thyroidal T4 and T3 secretion. This is especially true for women with thyroid cancer who have received radioiodine therapy [56] or patients with postablative or surgical hypothyroidism for Graves' disease or goiter [62]. Several factors have been thought to be responsible for the increased T4 requirement during pregnancy. They include weight gain and increased T4 pool size, high serum thyroxine-binding globulin (TBG) concentrations, placental deiodinase activity (which increases clearance of T4), transfer of T4 to the fetus, and reduced gastrointestinal absorption due to iron in prenatal vitamins [55].

Monitoring — The T4 dose should be reduced to prepregnancy levels after delivery, but serum TSH should be measured four to six weeks later to confirm that the reduction was appropriate [4,55,63].

THYROID PEROXIDASE ANTIBODIES IN EUTHYROID WOMEN — An increased risk of fetal loss, perinatal mortality, and large-for-gestational-age infants has been reported in euthyroid women with high serum thyroid peroxidase (TPO) antibody concentrations. In addition, euthyroid women with TPO antibodies are at high risk for developing subclinical hypothyroidism in the first trimester and thyroiditis in the postpartum period.

The decision to treat euthyroid women with TPO antibodies with T4 or to monitor for the development of hypothyroidism during pregnancy is controversial. Treatment with T4 may improve miscarriage rates, but the data are conflicting. This issue is reviewed in detail elsewhere. (See 'Indications for treatment' above and "Overview of thyroid disease in pregnancy", section on 'Thyroid peroxidase antibodies in euthyroid women' and "Evaluation of couples with recurrent pregnancy loss" and "Management of couples with recurrent pregnancy loss", section on 'Thyroid dysfunction and diabetes mellitus'.)

In TPO-positive women who are not treated with T4, monitoring is suggested. We measure TSH every four weeks until mid-pregnancy (approximately 20 weeks) and at least once during the last trimester to monitor for the development of hypothyroidism.

SOCIETY GUIDELINE LINKS — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Hypothyroidism".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword (s) of interest.)

- Basics topics (see "Patient education: Congenital hypothyroidism (The Basics)")

SUMMARY AND RECOMMENDATIONS

- The range of clinical manifestations of hypothyroidism during pregnancy is similar to those that occur in nonpregnant patients and may include fatigue, cold intolerance, constipation, and weight gain. Symptoms may be overlooked or attributed to the pregnancy itself. Many patients are asymptomatic. Hypothyroidism can have additional adverse effects on the mother and child, depending upon the biochemical severity of the hypothyroidism. (See 'Clinical features' above and 'Pregnancy complications' above.)

- The diagnosis of overt primary hypothyroidism during pregnancy is based upon the finding of an elevated population and trimester-specific thyroid-stimulating hormone (TSH) concentration (or above 4.0 mU/L when local reference range is not available) in conjunction with a decreased free thyroxine (T4) concentration (below assay normal using reference range for pregnant women). Subclinical hypothyroidism is defined as an elevated population and trimester-specific serum TSH concentration and a normal free T4 concentration. (See 'Diagnosis' above.)

- The universal screening of asymptomatic pregnant women for thyroid dysfunction during the first trimester of pregnancy is controversial. We suggest a targeted approach (case finding) rather than universal screening (**Grade 2C**). We favor screening pregnant women if they are from an area of moderate to severe iodine insufficiency; have symptoms of hypothyroidism; have a family or personal history of thyroid disease or have a personal history of goiter, thyroid peroxidase (TPO) antibodies, type 1 diabetes or other autoimmune disorder, head and neck radiation, recurrent miscarriage or preterm delivery, morbid obesity, infertility, multiple prior pregnancies (>2), use of amiodarone, lithium, or recent iodinated radiocontrast; or age >30 years. (See 'Whom to screen' above.)

- In women who meet the case-finding criteria, we measure serum TSH during the first trimester as the screening test for hypothyroidism. If the serum TSH is above 2.5 mU/L, we also measure TPO antibodies, and if the TSH is above the population and trimester-specific upper limit of normal (or >4 mU/L if local reference range is not available), we measure free T4 to determine the degree of hypothyroidism. (See 'Approach to screening' above.)

- In women with normal TSH at initial screening but at particularly high risk for developing hypothyroidism during pregnancy (TPO antibody positive, post-radioiodine treatment, post-hemithyroidectomy, history of childhood exposure to high-dose irradiation of the head or neck region), we reassess TSH during pregnancy (eg, approximately every four weeks during the first trimester, and then once during each of the second and third trimesters). (See 'Approach to screening' above.)

- All pregnant women with newly diagnosed, overt hypothyroidism (TSH above population and trimester-specific normal reference range [or above 4.0 mU/L when local reference range is not available] with low free T4) should be treated with thyroid hormone (levothyroxine, T4). In addition, we suggest initiating T4 replacement in pregnant women with subclinical hypothyroidism (TSH above population and trimester-specific normal reference range [or above 4.0 mU/L] with normal free T4) (**Grade 2B**). (See 'Indications for treatment' above and 'Subclinical hypothyroidism' above.)

  Patients with overt hypothyroidism should be started on close to full replacement doses (1.6 mcg/kg body weight per day), while patients with subclinical hypothyroidism may become euthyroid with lower doses and can therefore be started on approximately 1 mcg/kg daily. TSH should be measured every four weeks during the first half of pregnancy because dose adjustments are often required. The goal of treatment is to maintain TSH in the lower half of the trimester-specific reference range (or approximately <2.5 mU/L). (See 'Levothyroxine initial dosing' above and 'Monitoring and dose adjustments' above.)

- An increased rate of fetal loss and premature delivery has been reported in women with high serum anti-TPO antibody concentrations, and adverse outcomes occur at a lower TSH than in women without TPO antibodies. For pregnant women with a TSH between 2.6 and 4 mU/L, positive TPO antibodies, and a history of recurrent miscarriage, we suggest treatment with T4 (**Grade 2C**), typically 50 mcg daily. For pregnant women with TSH in this range and no prior history of miscarriage, we individualize the decision to treat based upon the presence of TPO antibodies and patient values and preferences. (See 'Indications for treatment' above and "Overview of thyroid disease in pregnancy", section on 'Thyroid peroxidase antibodies in euthyroid women' and "Management of couples with recurrent pregnancy loss", section on 'Thyroid dysfunction and diabetes mellitus'.)

- Women with preexisting hypothyroidism who are planning to become pregnant should optimize their thyroid hormone dose preconception. The goal preconception serum TSH level is between the lower reference limit and 2.5 mU/L. If possible, women already taking levothyroxine should have a normal serum TSH (ie, <2.5 mU/L) prior to becoming pregnant. (See 'Goal preconception TSH' above.)

- T4 dose requirements may increase during pregnancy in women with preexisting overt or subclinical hypothyroidism. For treated hypothyroid women who are newly pregnant, we suggest preemptively increasing their levothyroxine dose at the time of the positive pregnancy test (**Grade 2B**). We typically accomplish this by increasing the dose from once-daily dosing to a total of nine doses per week (double the daily dose two days each week). (See 'Preexisting hypothyroidism' above.)

  An alternative to preemptively increasing the dose is to measure serum TSH as soon as pregnancy is confirmed, then again four weeks later, four weeks after any change in the dose of T4, and at least once each trimester. The dose should be adjusted as needed every four weeks to achieve a normal TSH level, using a trimester-specific reference range. (See "Treatment of primary hypothyroidism in adults", section on 'Initial monitoring and dose adjustments'.)

REFERENCES

1. Allan WC, Haddow JE, Palomaki GE, et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. J Med Screen 2000; 7:127.
2. Casey BM, Dashe JS, Spong CY, et al. Perinatal significance of isolated maternal hypothyroxinemia identified in the first half of pregnancy. Obstet Gynecol 2007; 109:1129.
3. Liu H, Shan Z, Li C, et al. Maternal subclinical hypothyroidism, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study. Thyroid 2014; 24:1642.
4. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid 2017; 27:315.
5. GOLDSMITH RE, STURGIS SH, LERMAN J, STANBURY JB. The menstrual pattern in thyroid disease. J Clin Endocrinol Metab 1952; 12:846.
6. Abalovich M, Gutierrez S, Alcaraz G, et al. Overt and subclinical hypothyroidism complicating pregnancy. Thyroid 2002; 12:63.
7. Krassas GE, Pontikides N, Kaltsas T, et al. Disturbances of menstruation in hypothyroidism. Clin Endocrinol (Oxf) 1999; 50:655.
8. Hallengren B, Lantz M, Andreasson B, Grennert L. Pregnant women on thyroxine substitution are often dysregulated in early pregnancy. Thyroid 2009; 19:391.
9. LaFranchi SH, Haddow JE, Hollowell JG. Is thyroid inadequacy during gestation a risk factor for adverse pregnancy and developmental outcomes? Thyroid 2005; 15:60.
10. Leung AS, Millar LK, Koonings PP, et al. Perinatal outcome in hypothyroid pregnancies. Obstet Gynecol 1993; 81:349.
11. Wasserstrum N, Anania CA. Perinatal consequences of maternal hypothyroidism in early pregnancy and inadequate replacement. Clin Endocrinol (Oxf) 1995; 42:353.
12. Davis LE, Leveno KJ, Cunningham FG. Hypothyroidism complicating pregnancy. Obstet Gynecol 1988; 72:108.
13. Stagnaro-Green A, Chen X, Bogden JD, et al. The thyroid and pregnancy: a novel risk factor for very preterm delivery. Thyroid 2005; 15:351.
14. Pop VJ, Kuijpens JL, van Baar AL, et al. Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. Clin Endocrinol (Oxf) 1999; 50:149.
15. Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999; 341:549.
16. Männistö T, Mendola P, Grewal J, et al. Thyroid diseases and adverse pregnancy outcomes in a contemporary US cohort. J Clin Endocrinol Metab 2013; 98:2725.
17. Idris I, Srinivasan R, Simm A, Page RC. Maternal hypothyroidism in early and late gestation: effects on neonatal and obstetric outcome. Clin Endocrinol (Oxf) 2005; 63:560.
18. Willoughby KA, McAndrews MP, Rovet JF. Effects of maternal hypothyroidism on offspring hippocampus and memory. Thyroid 2014; 24:576.
19. Klein RZ, Haddow JE, Faix JD, et al. Prevalence of thyroid deficiency in pregnant women. Clin Endocrinol (Oxf) 1991; 35:41.

20. Casey BM, Dashe JS, Wells CE, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol 2005; 105:239.
21. Wilson KL, Casey BM, McIntire DD, et al. Subclinical thyroid disease and the incidence of hypertension in pregnancy. Obstet Gynecol 2012; 119:315.
22. Schneuer FJ, Nassar N, Tasevski V, et al. Association and predictive accuracy of high TSH serum levels in first trimester and adverse pregnancy outcomes. J Clin Endocrinol Metab 2012; 97:3115.
23. Korevaar TI, Schalekamp-Timmermans S, de Rijke YB, et al. Hypothyroxinemia and TPO-antibody positivity are risk factors for premature delivery: the generation R study. J Clin Endocrinol Metab 2013; 98:4382.
24. Breathnach FM, Donnelly J, Cooley SM, et al. Subclinical hypothyroidism as a risk factor for placental abruption: evidence from a low-risk primigravid population. Aust N Z J Obstet Gynaecol 2013; 53:553.
25. Negro R, Schwartz A, Gismondi R, et al. Increased pregnancy loss rate in thyroid antibody negative women with TSH levels between 2.5 and 5.0 in the first trimester of pregnancy. J Clin Endocrinol Metab 2010; 95:E44.
26. Cleary-Goldman J, Malone FD, Lambert-Messerlian G, et al. Maternal thyroid hypofunction and pregnancy outcome. Obstet Gynecol 2008; 112:85.
27. Maraka S, Ospina NM, O'Keeffe DT, et al. Subclinical Hypothyroidism in Pregnancy: A Systematic Review and Meta-Analysis. Thyroid 2016; 26:580.
28. Baker VL, Rone HM, Pasta DJ, et al. Correlation of thyroid stimulating hormone (TSH) level with pregnancy outcome in women undergoing in vitro fertilization. Am J Obstet Gynecol 2006; 194:1668.
29. Li Y, Shan Z, Teng W, et al. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25-30 months. Clin Endocrinol (Oxf) 2010; 72:825.
30. Smit BJ, Kok JH, Vulsma T, et al. Neurologic development of the newborn and young child in relation to maternal thyroid function. Acta Paediatr 2000; 89:291.
31. Fan X, Wu L. The impact of thyroid abnormalities during pregnancy on subsequent neuropsychological development of the offspring: a meta-analysis. J Matern Fetal Neonatal Med 2016; 29:3971.
32. Williams F, Watson J, Ogston S, et al. Mild maternal thyroid dysfunction at delivery of infants born ≤34 weeks and neurodevelopmental outcome at 5.5 years. J Clin Endocrinol Metab 2012; 97:1977.
33. Nazarpour S, Ramezani Tehrani F, Simbar M, et al. Effects of levothyroxine treatment on pregnancy outcomes in pregnant women with autoimmune thyroid disease. Eur J Endocrinol 2017; 176:253.
34. Lazarus JH, Bestwick JP, Channon S, et al. Antenatal thyroid screening and childhood cognitive function. N Engl J Med 2012; 366:493.
35. Negro R, Schwartz A, Gismondi R, et al. Universal screening versus case finding for detection and treatment of thyroid hormonal dysfunction during pregnancy. J Clin Endocrinol Metab 2010; 95:1699.
36. Casey BM, Thom EA, Peaceman AM, et al. Treatment of Subclinical Hypothyroidism or Hypothyroxinemia in Pregnancy. N Engl J Med 2017; 376:815.
37. Kooistra L, Crawford S, van Baar AL, et al. Neonatal effects of maternal hypothyroxinemia during early pregnancy. Pediatrics 2006; 117:161.
38. Henrichs J, Bongers-Schokking JJ, Schenk JJ, et al. Maternal thyroid function during early pregnancy and cognitive functioning in early childhood: the generation R study. J Clin Endocrinol Metab 2010; 95:4227.
39. Finken MJ, van Eijsden M, Loomans EM, et al. Maternal hypothyroxinemia in early pregnancy predicts reduced performance in reaction time tests in 5- to 6-year-old offspring. J Clin Endocrinol Metab 2013; 98:1417.
40. Ghassabian A, El Marroun H, Peeters RP, et al. Downstream effects of maternal hypothyroxinemia in early pregnancy: nonverbal IQ and brain morphology in school-age children. J Clin Endocrinol Metab 2014; 99:2383.
41. Román GC, Ghassabian A, Bongers-Schokking JJ, et al. Association of gestational maternal hypothyroxinemia and increased autism risk. Ann Neurol 2013; 74:733.
42. Modesto T, Tiemeier H, Peeters RP, et al. Maternal Mild Thyroid Hormone Insufficiency in Early Pregnancy and Attention-Deficit/Hyperactivity Disorder Symptoms in Children. JAMA Pediatr 2015; 169:838.
43. Craig WY, Allan WC, Kloza EM, et al. Mid-gestational maternal free thyroxine concentration and offspring neurocognitive development at age two years. J Clin Endocrinol Metab 2012; 97:E22.
44. Blatt AJ, Nakamoto JM, Kaufman HW. National status of testing for hypothyroidism during pregnancy and postpartum. J Clin Endocrinol Metab 2012; 97:777.
45. Vaidya B, Hubalewska-Dydejczyk A, Laurberg P, et al. Treatment and screening of hypothyroidism in pregnancy: results of a European survey. Eur J Endocrinol 2012; 166:49.
46. Horacek J, Spitalnikova S, Dlabalova B, et al. Universal screening detects two-times more thyroid disorders in early pregnancy than targeted high-risk case finding. Eur J Endocrinol 2010; 163:645.

47. Lepoutre T, Debiève F, Gruson D, Daumerie C. Reduction of miscarriages through universal screening and treatment of thyroid autoimmune diseases. Gynecol Obstet Invest 2012; 74:265.
48. Committee on Patient Safety and Quality Improvement, Committee on Professional Liability. ACOG Committee Opinion No. 381: Subclinical hypothyroidism in pregnancy. Obstet Gynecol 2007; 110:959.
49. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2012; 97:2543.
50. Vaidya B, Anthony S, Bilous M, et al. Detection of thyroid dysfunction in early pregnancy: Universal screening or targeted high-risk case finding? J Clin Endocrinol Metab 2007; 92:203.
51. Brent GA. Diagnosing thyroid dysfunction in pregnant women: Is case finding enough? J Clin Endocrinol Metab 2007; 92:39.
52. Thung SF, Funai EF, Grobman WA. The cost-effectiveness of universal screening in pregnancy for subclinical hypothyroidism. Am J Obstet Gynecol 2009; 200:267.e1.
53. Dosiou C, Barnes J, Schwartz A, et al. Cost-effectiveness of universal and risk-based screening for autoimmune thyroid disease in pregnant women. J Clin Endocrinol Metab 2012; 97:1536.
54. Shields BM, Knight BA, Hill AV, et al. Five-year follow-up for women with subclinical hypothyroidism in pregnancy. J Clin Endocrinol Metab 2013; 98:E1941.
55. Kaplan MM. Management of thyroxine therapy during pregnancy. Endocr Pract 1996; 2:281.
56. Alexander EK, Marqusee E, Lawrence J, et al. Timing and magnitude of increases in levothyroxine requirements during pregnancy in women with hypothyroidism. N Engl J Med 2004; 351:241.
57. Vadiveloo T, Mires GJ, Donnan PT, Leese GP. Thyroid testing in pregnant women with thyroid dysfunction in Tayside, Scotland: the thyroid epidemiology, audit and research study (TEARS). Clin Endocrinol (Oxf) 2013; 78:466.
58. Abalovich M, Alcaraz G, Kleiman-Rubinsztein J, et al. The relationship of preconception thyrotropin levels to requirements for increasing the levothyroxine dose during pregnancy in women with primary hypothyroidism. Thyroid 2010; 20:1175.
59. Ashoor G, Rotas M, Maiz N, et al. Maternal thyroid function at 11-13 weeks of gestation in women with hypothyroidism treated by thyroxine. Fetal Diagn Ther 2010; 28:22.
60. Taylor PN, Minassian C, Rehman A, et al. TSH levels and risk of miscarriage in women on long-term levothyroxine: a community-based study. J Clin Endocrinol Metab 2014; 99:3895.
61. Yassa L, Marqusee E, Fawcett R, Alexander EK. Thyroid hormone early adjustment in pregnancy (the THERAPY) trial. J Clin Endocrinol Metab 2010; 95:3234.
62. Loh JA, Wartofsky L, Jonklaas J, Burman KD. The magnitude of increased levothyroxine requirements in hypothyroid pregnant women depends upon the etiology of the hypothyroidism. Thyroid 2009; 19:269.
63. Roti E, Minelli R, Salvi M. Clinical review 80: Management of hyperthyroidism and hypothyroidism in the pregnant woman. J Clin Endocrinol Metab 1996; 81:1679.

Topic 16609 Version 16.0

Contributor Disclosures

Douglas S Ross, MD Consultant/Advisory Board: Novo Nordisk [Thyroid cancer]; Medullary Thyroid Cancer Registry Consortium [Thyroid cancer]. **David S Cooper, MD** Nothing to disclose **Charles J Lockwood, MD, MHCM** Consultant/Advisory Boards: Celula [Aneuploidy screening (No current products or drugs in the US)]. **Jean E Mulder, MD** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy