



The Diagnosis and Management of Thyroid Disease: Interface of the Endocrinologist, Obstetrician, and Primary Care Physician

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Introduction

Thyroid disease is relatively common in the US population, and its prevalence increases with age. In the third National Health and Nutrition Survey (NHANES III), conducted between 1988 and 1994, subclinical or overt hyperthyroidism was present in 1.3% of the US population, and subclinical or overt hypothyroidism in 4.6%.¹ In a sample of Framingham Heart Study subjects over age 60, 3.9% had suppressed serum thyroid stimulating hormone (TSH) values consistent with hyperthyroidism,² while 10.3% had some degree of hypothyroidism, as evidenced by elevated serum TSH levels (>5 $\mu\text{IU/mL}$).³ In the largest cross-sectional study to date, Canaris et al examined thyroid function tests from 25 862 participants in a statewide health fair in Colorado.⁴ They documented elevated serum TSH levels in 9.5% of this population and suppressed serum TSH levels in 2.2%. Nodular thyroid disease also is highly prevalent in the general population: a series of consecutive autopsies performed at the Mayo Clinic demonstrated the presence of thyroid nodules in 50.5% of patients without a history of clinically detectable thyroid disease.⁵

Primary care physicians and obstetrician-gynecologists play an essential role in the diagnosis of thyroid disorders and, frequently, in their management. A collaborative relationship between endocrinologists and referring physicians is critical. The appropriate use of screening tests coupled with a basic understanding of thyroid function tests (especially of normal physiologic changes in the settings of acute illness, pregnancy, and the postpartum period) is necessary to differentiate true thyroid pathology and to determine whether further testing or referral to an endocrinologist is warranted. Although various clinical guidelines for the screening and treatment of thyroid diseases have been proposed,⁶⁻¹¹ published algorithms have not always been in agreement.¹² Additionally, many medications commonly prescribed by primary care physicians and obstetrician-gynecologists have important effects on thyroid function and thyroid function tests. Good communication between providers is crucial to prevent missed diagnoses, mismanagement, unnecessary testing, or inappropriate referrals.

The following 3 patients were recently referred to our endocrine clinic and demonstrate some of the problems commonly encountered in the evaluation and management of thyroid disease:

Case 1

A 30-year-old woman presented to her obstetrician at 10 weeks gestation for routine antenatal care. She complained of significant nausea and vomiting. A screening TSH level was <0.01 $\mu\text{IU/mL}$ (normal 0.35-5.50 $\mu\text{IU/mL}$). Peripheral thyroid hormone tests were not obtained. The patient had no personal or family history of thyroid disease. The nausea and vomiting resolved after the first trimester of pregnancy. The obstetrician ordered follow-up thyroid function tests at 36 weeks gestation, when the patient complained of intermittent palpitations. Propylthiouracil (PTU) 100 mg TID was started the day the tests were sent. TSH was 0.49 $\mu\text{IU/mL}$, total thyroxine (T_4) was 13.7 $\mu\text{g/dL}$ (normal 4.5-10.9 $\mu\text{g/dL}$), and free T_4 was 0.84 ng/dL (normal, 0.89-1.80 ng/dL). The patient was referred to an endocrinologist and was seen 2 days later. The PTU was stopped. A healthy baby was delivered at 38 weeks gestation.

Case 2

A 30-year-old man presented to an urgent care clinic complaining of fever and cough. A chest film demonstrated clear lung fields, but tracheal deviation to the right was noted. The radiology report stated that "further evaluation of this finding is recommended, to include CT study." The patient followed up with his primary care physician, who sent him for a CT scan of the neck with contrast. On the same day, the following laboratory studies were obtained: TSH, 1.23 $\mu\text{IU/mL}$; total triiodothyronine (T_3), 146 ng/dL (normal 60-180 ng/dL); T_4 , 9.0 $\mu\text{g/dL}$; free T_4 , 0.88 ng/dL; and free T_4 index, 2.1 (normal 1.0-4.0). The radiologist reported a 5-cm well-circumscribed mass extending from the left lobe of the thyroid, and recommended correlation with nuclear thyroid scan. A ^{123}I thyroid uptake and scan was obtained, which showed a 24-hour uptake of 9%, although the radiologist noted that "true uptake could be different in light of patient's recent administration of

iodinated contrast media." The scan showed multiple "cold" nodules within an enlarged left thyroid lobe. At this point, the patient was referred to an endocrinologist for further work-up.

Case 3

A 52-year-old woman with a history of HIV and hepatitis C was referred to endocrinology for care of her type 2 diabetes. Her medication list included Prempro® and methimazole (MMI). The patient was unclear about her thyroid history. A review of her records revealed that she had presented to her primary care physician 2 years earlier with a complaint of weight loss. At that time, the serum TSH was normal at 1.11 $\mu\text{IU/mL}$ and the total T_4 was elevated to 15.9 $\mu\text{g/dL}$. Based on these laboratory results, she was started on 10 mg of daily MMI. Follow-up serum TSH was 9.42 $\mu\text{IU/mL}$ after 4 months of the MMI. After 8 months, the serum TSH was 67.01 $\mu\text{IU/mL}$ and the patient complained of fatigue; after obtaining this value, the patient's MMI was stopped and she was started on 100 μg of levothyroxine sodium (LT_4) daily. However, the LT_4 was discontinued shortly thereafter. At the patient's next visit, the serum TSH was 2.35 $\mu\text{IU/mL}$, the total T_3 was 276 ng/dL , and the free T_4 index was 1.02. Based on these laboratory results, the MMI was re-started at 20 mg daily. After 4 months on this dose, her serum TSH was 45.68 $\mu\text{IU/mL}$ and her free T_4 was 0.5 ng/dL . Once again, the MMI was transiently stopped and then restarted. The MMI was discontinued immediately by the patient's endocrinologist.

These cases are meant to illustrate the miscommunication and inappropriate management of thyroid disease that frequently occurs, even in academic settings. The first case is that of a woman who probably had gestational thyrotoxicosis that resolved after the first trimester of pregnancy. Timely follow-up thyroid function tests were not obtained and she was inappropriately treated later in pregnancy with antithyroid medications. The second case is an example of an extraordinarily costly work-up of a thyroid nodule. The primary care physician in this case incurred unnecessary costs by adopting all of the radiologist's suggestions for further imaging. It is our experience that radiologists frequently recommend unnecessary thyroid imaging. In addition, the iodinated contrast study was relatively contraindicated in this patient because of the risk of provoking iodine-induced hyperthyroidism in an autonomous nodule and because of the subsequent difficulty in obtaining nuclear medicine imaging, if needed. The third case is that of a woman inappropriately treated with MMI for elevated total T_4 values in the setting of a normal serum TSH and free T_4 . The elevated total T_3 and T_4 in this case were due to ele-

vated thyroid hormone binding globulin concentrations from the hepatitis and from Prempro®. True hyperthyroidism was never documented. She became repeatedly symptomatically hypothyroid on this regimen. Better communication among providers and understanding of basic thyroid physiology could have prevented the errors observed in the care of these 3 patients.

Screening for Thyroid Dysfunction

Thyroid function tests are clearly indicated in patients with signs or symptoms attributable to hypo- or hyperthyroidism. A serum TSH level is the most cost-effective initial test for thyroid dysfunction.¹³ If the serum TSH value falls outside the normal range, then other thyroid function tests (especially some measure of the free T_4 concentration) should be obtained.

The question of whether primary care physicians should screen for thyroid dysfunction in asymptomatic patients has been controversial. In 1998, the American College of Physicians recommended obtaining screening TSH levels in asymptomatic women over age 50, but not in men or in younger women.⁸ In 2000 the American Thyroid Association advocated the screening of all adults age 35 years or over with serum TSH measurements every 5 years.¹⁰ This approach has been found to be cost-effective, particularly in women.¹⁴ We believe that these recommendations are somewhat arbitrary but that serum TSH testing should be carried out in postmenopausal women on a regular basis.

More frequent thyroid screening is indicated in patients with known risk factors for thyroid disease such as the presence of a goiter, a history of diabetes mellitus, previous thyroid surgery or neck radiation, pernicious anemia, premature gray hair, vitiligo, or any previous history or family history of thyroid disease. Additionally, any patient with an unexplained laboratory abnormality such as hypercholesterolemia, hyponatremia, anemia, hypercalcemia, or creatinine kinase elevation warrants a serum TSH level.¹⁰ Patients with new onset atrial fibrillation should also be tested, because approximately 15% will be hyperthyroid.^{15,16} Patients being treated with iodine-containing medications should be evaluated for thyroid dysfunction since excess iodine ingestion may induce hypothyroidism, especially in patients with Hashimoto thyroiditis. Less commonly in the US, iodine-containing medications may cause hyperthyroidism, especially in patients with multinodular goiter.¹⁷ Finally, patients with depression should be evaluated for hypothyroidism, since autoimmune thyroid disease is present in at least 15% of depressed patients¹⁹ and depression and cognitive

dysfunction may be due to hypothyroidism.

Screening should not be performed in the setting of severe nonthyroidal illness unless there is a strong clinical suspicion of thyroid dysfunction. In severely ill patients, serum T_3 concentrations decrease and reverse T_3 concentrations increase due to inhibition of the 5' monodeiodinase. Serum TSH levels may fall during acute illness and then transiently rise to above-normal levels during recovery. These physiologic changes may result in thyroid function tests that are very difficult to interpret.

Elevated thyroid autoantibodies, both to thyroid peroxidase (TPO) and, less frequently, to thyroglobulin (Tg), are common, especially in older women (approximately 25% of US women over age 60).¹ The prevalence of autoantibodies is much lower in African Americans.¹ Because elevated antibody levels may be present in euthyroid patients as well as in those with abnormal thyroid function,^{19,20} they are not useful as a primary screening test for hypothyroidism, but are useful to confirm the presence of Hashimoto disease as the cause of hypothyroidism and/or goiter after the diagnosis has been established.

Hypothyroidism

In the United States and other regions where dietary iodine is sufficient, Hashimoto's thyroiditis is the most common cause of hypothyroidism. In overt hypothyroidism, serum TSH levels are elevated and total and free T_4 levels are decreased. Only when hypothyroidism is severe does the serum T_3 fall below the normal range. Patients are usually symptomatic. Subclinical hypothyroidism is defined as the presence of an elevated serum TSH level with peripheral thyroid hormones (free T_3 and T_4) in the normal range. Signs and symptoms, if present, are subtle.

The majority of patients with hypothyroidism are readily managed by their primary care physicians. Consultation with an endocrinologist should be considered if central hypothyroidism is suspected, or if there is any difficulty in maintaining the serum TSH level in the normal range. Levothyroxine sodium (LT_4) is the treatment of choice. Clinicians also treat patients with subclinical hypothyroidism and elevated serum thyroid antibody concentrations because progression to overt hypothyroidism is far more common in those patients than in patients with negative thyroid antibodies.²¹ Treatment may also decrease the risk for hyperlipidemia and atherosclerotic heart disease, which have been shown to be more prevalent in patients with subclinical hypothyroidism.^{22,23} The goal of LT_4 replacement therapy in either patients with either overt or subclinical hypothyroidism is the normalization of

serum TSH values. Recent evidence has suggested that the upper limit of normal for the serum TSH is approximately 2.5 μ U/mL in normal individuals without underlying thyroid disease and in the absence of medications known to affect thyroid function.²⁴

Communication between physicians regarding patient medications is important for patients on taking LT_4 therapy. Many medications, including amiodarone, lithium, and interferon alpha, are known to affect thyroid function, causing either hyperthyroidism or hypothyroidism. Other medications may alter thyroid function tests without inducing thyroid dysfunction. One of the most commonly prescribed substances is estrogen. Even low-dose estrogen increases serum levels of thyroxine-binding globulin (TBG), the principal thyroid hormone binding protein,²⁵ due to decreased hepatic clearance of a more heavily sialylated TBG.²⁶ Therefore, euthyroid patients on hormone replacement therapy or oral contraceptives will generally have elevated total T_3 and T_4 values, while serum TSH, free T_3 , and free T_4 levels remain unchanged. Tamoxifen, a selective estrogen receptor modulator (SERM) with estrogen-like effects on the liver, has been reported to behave like estrogen in increasing serum TBG levels in postmenopausal breast cancer patients.^{27,28} Raloxifene (Evista[®]) also increases serum TBG.²⁹ Hypothyroid women who are being treated with LT_4 therapy often require an increase in the LT_4 doses if an oral contraceptive, estrogen replacement, or perhaps a SERM is prescribed.³⁰ A wide variety of medications and clinical situations may affect the administered dose of LT_4 and are summarized in Tables 1 and 2.

Thyrotoxicosis

In general, once hyperthyroidism is detected, patients should be referred to an endocrinologist, as the diagnosis and management of their thyroid disease is often complex. Overt thyrotoxicosis is generally symptomatic; laboratory values will consist of a suppressed serum TSH value with serum T_3 , free T_3 , T_4 , and free T_4 values above the normal range. Subclinical hyperthyroidism generally is asymptomatic or causes only mild symptoms. It is a biochemical diagnosis, in which the serum TSH value is below the normal range, but often detectable, and peripheral thyroid hormone values are normal.

In iodine-sufficient regions Graves disease is the most common cause of hyperthyroidism. Hyperthyroidism may also be caused by multinodular goiter (Plummers disease), in which one or more nodules gradually develop autonomy, often leading to subclinical and then to overt hyperthyroidism.³¹ Hyperthyroidism may

be precipitated in patients with autonomous nodules by the administration of iodine in the form of radiocontrast agents, amiodarone, or other iodine-containing medications. Iatrogenic thyrotoxicosis can result from overzealous thyroid hormone replacement therapy for hypothyroidism, or from TSH-suppressive doses of LT_4 for thyroid cancer. Finally, thyrotoxicosis may be caused by thyroiditis, in which excess stored thyroid hormone is released from a damaged gland.

Once hyperthyroidism has been identified, the radioiodine uptake (RAIU) and scan may be used to help distinguish among these etiologies. The thyroid RAIU is elevated in Graves disease. It may be low, normal, or mildly elevated in patients with a toxic multinodular goiter. It will be low in patients with thyrotoxicosis due to exogenous LT_4 administration, or due to thyrotoxic phase of thyroiditis, but the serum Tg will be low in the former case and elevated in the latter. A scan may be helpful in differentiating between Graves disease (diffuse uptake) and toxic multinodular goiter (one or more focal areas of increased uptake).³² Graves disease is an autoimmune disorder that is generally characterized by the presence of TPO. Less frequently, the disorder is associated with Tg antibodies. Graves disease is also associated with the presence of an immunoglobulin detected in vitro by the stimulation of cAMP in thyroid cells (thyroid-stimulating immunoglobulin, TSI) or another immunoglobulin detected by the displacement of TSH from cell membranes (TSH-binding inhibitory immunoglobulin, TBII).

Patients with overt hyperthyroidism from Graves disease or from toxic multinodular goiter should clearly be treated. One therapeutic option is medical management with MMI or PTU, both of which decrease thyroid hormone synthesis. Therapy with 1 of these drugs will induce long-term remission of Graves disease in about half of all patients.³³ Since remission of the hyperthyroidism due to toxic multinodular goiter almost never occurs, therapy with MMI or PTU is only given prior to definitive therapy, as described below. Side effects of both of these medications include rash or urticaria. More seriously, agranulocytosis occurs in approximately 0.3% of patients.¹¹ Patients starting on these medications should be cautioned to discontinue use and contact their physician if they develop fever, rash, jaundice, arthralgia, or sore throat.

More definitive therapy with radioactive iodine may also be elected, especially in older patients. After radioactive iodine treatment, patients may become transiently more thyrotoxic, because of damage to the gland and release of the stored hormone. Pretreatment with antithyroid medications may help protect older patients or other patients at risk for cardiac complications, by decreasing thyroid hormone

stores,¹¹ although this concept has recently been challenged.^{34,35} Most patients will become euthyroid within a few months after receiving a single large dose of radioiodine, while the remaining 10%-20% of patients require retreatment 6 months to 1 year later. Within 1 year of treatment, up to 90% of patients will become hypothyroid; the other 10% become hypothyroid at a rate of 2%-3% per year.³³

Surgery is another option for treatment of younger patients with hyperthyroidism. It is especially useful for patients with very large goiters and/or compressive symptoms who often require multiple doses of ^{131}I . Subtotal thyroidectomy, which leaves a few grams of thyroid tissue in place, is the procedure of choice. The most common adverse effects of thyroidectomy are injury to the parathyroids, resulting in hypocalcemia, and injury to the recurrent laryngeal nerve. Patients should be treated with antithyroid drugs to restore euthyroidism prior to the operation. Additionally, they should receive iodine for 7 to 10 days before surgery to decrease thyroid blood flow.

Beta-blockers can be used as adjunctive treatment to slow the heart rate and improve symptoms of anxiety, tremor, palpitations, heat intolerance, and tremor. Beta blockade should be used as a primary therapy only in patients with transient thyrotoxicosis secondary to thyroiditis who have a low thyroid RAIU.¹¹

After patients become biochemically euthyroid, symptoms of hyperthyroidism should resolve within a few weeks. Patients with atrial fibrillation in the setting of hyperthyroidism will often spontaneously convert to sinus rhythm once the hyperthyroidism has been corrected, generally within 4 months of normalization of serum T_3 and T_4 concentrations.³⁶ Anticoagulant therapy has been advised in most patients with thyrotoxic atrial fibrillation.³⁷

The question of whether subclinical hyperthyroidism should be treated remains controversial.³⁸ When a persistently suppressed TSH level has been documented, the goal of therapy is to normalize the serum TSH using small doses of MMI or PTU. Definitive therapy with ^{131}I may be carried out, especially in patients with goiter. If the serum TSH is low during therapy for hypothyroidism (in nonthyroid cancer patients), the dose of LT_4 should be decreased every 3-4 months until the serum TSH normalizes. Treatment of subclinical hyperthyroidism may decrease the risk for atrial fibrillation.^{38,39} Treatment with anti-thyroid drugs has also been shown to have a beneficial effect on osteoporosis in two small studies.^{40,41} However, women with untreated subclinical hyperthyroidism have not been shown to have a significant difference in fracture rate,⁴² and subclinical hyperthyroidism has not been

shown to have detrimental effects on bone in men or premenopausal women. Some authors^{43,44} advocate aggressive treatment for subclinical hyperthyroidism, while others suggest a policy of watchful waiting, deferring treatment until the hyperthyroidism becomes clinically evident.

Nodules

Thyroid nodules are frequently detected by primary care providers during routine neck examinations. Given their high prevalence in the general population, thyroid nodules are also commonly noted as incidental findings on neck imaging. Nodules smaller than one centimeter usually can not be palpated and are most often detected by ultrasound, CT, or MRI examination. These nodules pose little risk to patients and may simply be monitored.⁴⁵ A serum TSH should be measured in patients with thyroid nodules. If the patient is euthyroid or hypothyroid, as is frequently the case, they should be referred to an endocrinologist promptly for fine needle aspiration biopsy (FNA) of the dominant nodule. Early referral for biopsy has been shown to be both efficient and cost-effective.⁴⁶

In patients with suppressed serum TSH levels, serum T₃ and free T₄ concentrations should be measured. Whether the hypothyroidism is subclinical or overt, a thyroid 123I or scan should be obtained. If all the uptake on the scan is in the nodule ("hot"), the patient should be referred to an endocrinologist for definitive therapy with ¹³¹I or, in younger patients, surgical removal of the nodule. If the nodule is hypofunctioning ("cool" or "cold") or functioning normally, the patient should be referred to an endocrinologist for an FNA.

Approximately 90% of biopsied nodules will prove to be benign.¹¹ Of the remainder, approximately 80% will be papillary carcinoma and 15% will prove to be follicular lesions. All follicular nodules require surgery, as follicular carcinoma can be differentiated from benign follicular adenoma only by histology. The therapy for both papillary and follicular carcinoma is total or near-total thyroidectomy, which may be followed by an ablative dose of radioactive iodine. Following surgery, LT₄ is usually given in TSH-suppressive doses. Overall, the 10-year survival is about 90% for papillary carcinoma and about 80% for follicular carcinoma, although the prognosis worsens for patients who are over age 60 at the time of diagnosis.^{47,48} Other thyroid neoplasms include anaplastic thyroid carcinoma, medullary carcinoma, lymphoma, and thyroid metastases from other primary neoplasms; these are all relatively rare.

Whether the growth of benign thyroid nodules or nontoxic colloid goiters should be suppressed with LT₄

remains controversial. We believe that nontoxic nodular goiter in older patients should not be treated with LT₄ because iatrogenic thyrotoxicosis due to autonomous nodules poses too great a risk. Furthermore, TSH-suppressive doses of LT₄ may induce cardiac abnormalities.⁵⁰

The Thyroid in Pregnant Women

It is particularly essential for obstetricians to understand the alterations of thyroid physiology and thyroid function tests in pregnant women. High estrogen levels increase the concentration of circulating TBG. Therefore, total T₃ and T₄ levels are increased throughout pregnancy, while free T₄ and free T₃ levels remain in the normal range except during the first trimester when they are high-normal or slightly elevated. Human chorionic gonadotropin (hCG) is a weak thyroid stimulator, binding to the TSH receptor. Thus, during the first trimester, when hCG levels are highest, serum TSH concentrations are often slightly below normal or at the low end of the normal range. Such physiologic gestational increased thyroid function is more common with twins or triplets and in women with morning sickness. Hyperemesis gravidarum may be accompanied by gestational thyrotoxicosis induced by a more bioactive hCG.⁵⁰ Except in the most severe cases this condition does not require antithyroid drug treatment, and resolves spontaneously as hCG levels fall after the 12th week of gestation.⁷

In general, the management of hyperthyroidism in pregnant women should be the purview of the endocrinologist. The diagnosis of hyperthyroidism may be more difficult in the setting of pregnancy, as symptoms such as fatigue, heat intolerance, and tachycardia are common to both conditions. In addition, definitive diagnosis is more difficult because nuclear thyroid scans are contraindicated in the pregnant patient. Once diagnosed, hyperthyroidism may be managed with PTU, with the goal of maintaining serum free T₄ levels in the high normal range.⁵¹ PTU has been preferred to MMI in pregnancy by most but not all endocrinologists due to the reported rare associations of MMI with aplasia cutis and gut abnormalities in the newborn.⁵²⁻⁵⁴ However, compliance is far better with MMI than with PTU, because patients can be managed with a single daily dose of MMI, in contrast to PTU, which requires multiple daily doses. Both PTU and MMI cross the placenta equally and may transiently decrease fetal thyroid function if given in excessive doses. Thyroidectomy, if required for refractory hyperthyroidism, is best performed in the second trimester. Graves disease frequently improves throughout gestation due to the immunosuppressive effects of pregnancy. However, thyroid-receptor stimulating antibody

ies cross the placenta (even in euthyroid pregnant women with Graves disease who have undergone thyroidectomy or radioactive iodine thyroid ablation prior to pregnancy), and should be measured in the third trimester. If the antibodies are present in high titer, the fetus and newborn should be followed closely for signs of Graves disease.

Women with pre-existing hypothyroidism frequently require increased doses of LT_4 during the first trimester and thereafter in order to maintain the serum TSH in the low-normal range and the serum free T_4 in the high-normal range.⁵⁵ The fetus does not produce its own thyroid hormone until week 10-12 of gestation; prior to that it is dependent on maternal T_4 that crosses the placenta in small quantities. The presence of thyroid hormone is critical for neural development. It has been demonstrated that IQ test scores are significantly decreased in the offspring of women with undiagnosed hypothyroidism during pregnancy.⁵⁶ Although routine screening for subclinical hypothyroidism during the first trimester has been advocated by some authors, this practice remains controversial. The 2002 guidelines of the American College of Obstetrics and Gynecology state that “there are insufficient data to warrant routine screening of asymptomatic pregnant women for hypothyroidism.”⁷ We advocate TSH testing in all women in the first trimester and LT_4 treatment for pregnant women with serum TSH levels that are not consistent with a normal pregnancy as described above.

When a thyroid nodule is detected in a pregnant woman, thyroid scan is contraindicated but FNA may be safely performed. However, thyroidectomy, if required, can be safely deferred until after delivery.⁵⁷

Conclusions

Thyroid disease is common in the general population. Routine screening for thyroid disease is performed primarily by primary care providers and obstetrician-gynecologists. Hypothyroidism can generally be diagnosed and managed by primary care providers, although confounding factors may occur that would necessitate referral. In most cases, patients with thyrotoxicosis or thyroid nodules should be referred promptly to an endocrinologist for management. Coordination of care between primary care providers, obstetrician-gynecologists, and endocrinologists is essential in order to provide optimal and cost-effective care for patients with thyroid disease.

Table 1. Drugs and clinical states that cause an increase in the maintenance dose of levothyroxine.

Decreased LT_4 Absorption
Malabsorption Syndromes
Jejunal bypass surgery
Short bowel syndrome
Cirrhosis
Drugs or Diet
Cholestyramine
Aluminum hydroxide
Carafate
Ferrous sulfate
Cation-exchange resin
High-fiber diet
Soy formula fed to infants
Calcium carbonate
Proton pump inhibitors in patients with achlorhydria
Raloxifene (?)
Increased Biliary Excretion
Dilantin
Rifampin
Phenobarbital
Carbamazepine
Decreased Deiodination of T_4 to T_3
Amiodarone
Unknown
Sertraline
Increased Serum Thyroid Hormone Binding Globulin
Pregnancy
Estrogen
Tamoxifen and other SERMs

Table 2. Drugs and clinical states which cause a decrease in the maintenance dose of levothyroxine

Decreased Serum Thyroid Hormone Binding Globulin
Androgens
Old Age
Weight Loss

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