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REVIEW ARTICLE

DRUG THERAPY

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The Management of Hyperthyroidism

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Hyperthyroidism is common, affecting approximately 2 percent of women and 0.2 percent of men¹. There are three principal treatments -- antithyroid drugs, radioiodine, and surgery -- all of which are effective, but opinions differ about the indications for them² because no single treatment regularly results in permanent euthyroidism.

Investigation of Hyperthyroidism

When **hyperthyroidism** is suspected, the diagnosis should be confirmed by measurement of serum thyrotropin and total or free thyroxine, which are usually present in low and high concentrations, respectively ([Figure 1](#))³. If the thyrotropin level is low but the thyroxine level is normal, serum triiodothyronine should be measured, since the patient may have triiodothyronine toxicosis. Serum total thyroxine concentrations are increased in patients with increased serum concentrations of thyroxine-binding globulin -- for example, pregnant women, persons taking estrogen, or persons who have an inherited increase in the production of thyroxine-binding globulin -- but serum concentrations of free thyroxine and thyrotropin are normal. The uncommon condition of familial dysalbuminemic hyperthyroxinemia, due to the presence of serum albumin with an abnormally high affinity for thyroxine, results in a spurious elevation of the free thyroxine concentration,⁴ as can a thyroxine-binding prealbumin (transthyretin) with abnormal affinity for thyroxine and the presence of thyroid hormone-binding autoantibodies⁵. All patients with these latter conditions are clinically euthyroid and have normal serum concentrations of thyrotropin.

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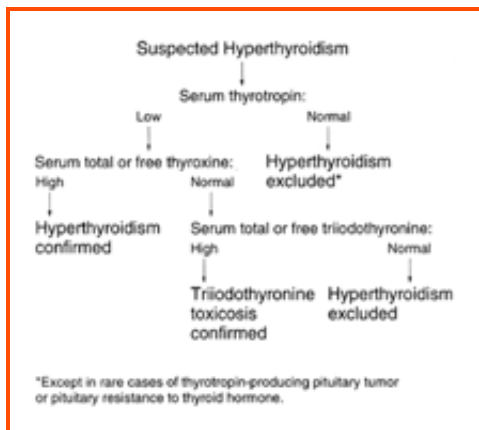


Figure 1. Scheme for Investigating Cases of Suspected **Hyperthyroidism**.

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The presence of normal serum thyrotropin concentrations nearly always excludes a diagnosis of **hyperthyroidism**⁶; the exception is the rare patient with **hyperthyroidism** caused by excessive thyrotropin secretion. The converse, however, is not true, since serum thyrotropin concentrations may be low in patients with nonthyroidal illness, patients taking certain drugs (glucocorticoids or dopamine),^{7,8} and some healthy elderly patients⁹.

Graves' disease is the most common cause of **hyperthyroidism** ([Table 1](#)). The diagnosis is obvious if a diffuse goiter and ophthalmopathy are present. Among other causes, a multinodular goiter, toxic thyroid adenoma, and subacute thyroiditis should be evident from the history and physical examination. If the cause is not obvious, then measurement of the uptake of radioiodine by the thyroid may be indicated; low values identify patients with silent or postpartum thyroiditis or iodine-induced thyrotoxicosis.

View this table: [Table 1.](#) Causes of **Hyperthyroidism**.

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Treatment may be directed at the cause of the **hyperthyroidism**, the thyroid hypersecretion, or the clinical manifestations of **hyperthyroidism** ([Table 2](#)). With respect to Graves' disease, only the latter two forms of treatment are feasible.

View this table: [Table 2.](#) Medical Treatment of **Hyperthyroidism**.

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Antithyroid Drugs

Methimazole, carbimazole, and propylthiouracil are the mainstays of antithyroid-drug therapy. Their principal action is to inhibit the organification of iodide and coupling of iodothyronines, and hence the synthesis of thyroid hormones. Propylthiouracil also inhibits the peripheral monodeiodination of thyroxine to triiodothyronine.

Methimazole is the active metabolite of carbimazole, and since the conversion of carbimazole to methimazole is virtually complete, their effects and equivalent doses are comparable. These drugs also reduce serum concentrations of thyrotropin-receptor antibodies and increase suppressor T-cell activity, suggesting that they have immunosuppressive actions,¹² although such changes may reflect control of **hyperthyroidism**. The half-life of methimazole in plasma is three to five hours, and that of propylthiouracil one to two hours¹³; thus, methimazole has a longer duration of action, although both drugs are effective for more than five hours because they accumulate in thyroid cells.

Indications for Antithyroid-Drug Therapy and Treatment Regimens

The three main drugs are prescribed for Graves' **hyperthyroidism** in the hope that the patient will have a remission of Graves' disease during therapy or to achieve euthyroidism before treatment with radioiodine or surgery. Our policy is to give an antithyroid drug in the hope of achieving remission in young patients (those 40 years old or younger) with a first episode of Graves' **hyperthyroidism**. In the case of older patients and young patients with relapse after a period of antithyroid-drug therapy, we give one of these drugs for only a short time before treating them with radioiodine.

If compliance is good, antithyroid drugs are highly effective in controlling **hyperthyroidism**. Methimazole (but not propylthiouracil) is effective if administered once daily,¹⁴ and serum thyroxine and triiodothyronine concentrations decrease more rapidly in patients treated with methimazole than in those treated with propylthiouracil¹⁵. These differences are slight, but because methimazole in moderate doses poses a lower risk of agranulocytosis, this drug is preferable to propylthiouracil.

Treatment is generally started with 10 to 20 mg of methimazole once a day or 75 to 100 mg of propylthiouracil three times a day. The dose should be reduced after four to six weeks as clinical and biochemical improvement occurs, and then adjusted every four to six weeks to maintain normal thyroid secretion until the maintenance dose is reached (methimazole, 5 to 10 mg a day; propylthiouracil, 50 to 100 mg a day) after approximately three months. The interval between follow-up visits can then be extended to three months. Because serum thyrotropin concentrations may remain low for weeks or months after serum thyroxine and triiodothyronine concentrations have returned to normal,^{6,16} measurements of serum thyrotropin alone during this interval are not helpful in adjusting treatment, except that elevated serum thyrotropin values indicate that the dose should be reduced. Although larger doses of methimazole or carbimazole lead to somewhat more rapid biochemical improvement than smaller doses, a single daily dose of 10 or 20 mg is sufficient to induce euthyroidism within several weeks; moreover, larger doses are associated with more side effects^{17,18,19}.

Side Effects

Serious side effects ([Table 3](#)) occur in approximately 3 of every 1000 patients, whether they receive methimazole or propylthiouracil, although a low dose of methimazole may be safer than either a high dose of methimazole or propylthiouracil with respect to agranulocytosis²⁰.

View this table: [Table 3. Side Effects of Antithyroid Drugs.](#)

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Agranulocytosis (indicated by a granulocyte count below 500 per cubic millimeter) is an idiosyncratic reaction to these drugs. It is more common among patients over 40 years old. Although this side effect is rarer among patients receiving less than 30 mg of methimazole a day²⁰ (there is no evidence that propylthiouracil has a dose effect), it can occur irrespective of the dose, age, or duration of treatment or during a second course of treatment²¹. Patients who have agranulocytosis commonly present with a fever or sore throat; patients should therefore be instructed to discontinue therapy and report these symptoms promptly if they occur. Since agranulocytosis develops rapidly, routine measurement of the white-cell count is usually not helpful, although in one study such measurement allowed agranulocytosis to be detected before the onset of symptoms²². Patients recover within two to three weeks after the drug is stopped, but some die despite appropriate isolation and prophylactic antibiotic therapy. Agranulocytosis is an absolute contraindication to further antithyroid-drug therapy, and treatment with radioiodine should be given. Jaundice, hepatitis or vasculitis, and lupus-like syndromes are other rare but serious complications that make the discontinuation of therapy mandatory. Propylthiouracil may cause a slight, transient increase in serum alanine aminotransferase concentrations, which will not necessitate a change in therapy²³.

The incidence of minor side effects such as pruritus and rash is similar with both methimazole and propylthiouracil; these problems may resolve despite continued therapy. If they are severe enough to alter treatment, methimazole can be substituted for propylthiouracil and vice versa, although cross-sensitivity to these drugs may occur.

Outcome of Treatment

There are conflicting results regarding the likelihood of a long-term remission of Graves' **hyperthyroidism** during antithyroid-drug therapy, with the reported rates ranging from 10 to 75 percent^{24,25,26}. Clinical findings associated (weakly) with remission are a small goiter and recent onset of the **hyperthyroidism**. There are no reliable tests for predicting relapse at the time that therapy is discontinued^{26,27,28,29,30,31,32}.

One factor that affects the likelihood of such remission is the duration of treatment²⁸. In one study, the rate of remission one year after treatment was stopped was 31 percent among patients treated for six months and 82 percent among patients treated for two years³³. Despite evidence in favor of longer treatment,³⁴ therapy is

usually continued for one to two years, after which the patient must be reevaluated regularly. I do not favor longer courses, because of the need for monitoring and poor compliance. Relapse is most likely within the first six months after withdrawal of therapy but may occur years later. If patients relapse and wish to avoid ablative treatment, antithyroid-drug therapy may be resumed; very-long-term therapy appears to be safe.

Evidence that antithyroid drugs have an immunosuppressive effect has led some clinicians to combine them with thyroxine replacement³⁵. A regimen of methimazole or carbimazole (30 mg a day) with thyroxine (100 to 200 μ g a day) prevents iatrogenic hypothyroidism and allows high-dose antithyroid-drug therapy to continue; concern about compliance and the advantages of this regimen, along with the contraindication to such therapy in pregnant women, has ensured that combination treatment has not been widely adopted. An exciting recent development in therapy for Graves' **hyperthyroidism** was the finding in a group of Japanese patients treated with methimazole for six months that the relapse rate among those given a combination of methimazole and thyroxine for a further year, followed by thyroxine therapy alone for three years, was 1.7 percent, as compared with 34.7 percent among those not given thyroxine³⁶. The low relapse rate may reflect thyroxine-induced suppression of thyrotropin secretion and diminished presentation of thyroid antigens, which thereby minimize the autoimmune response, although thyroxine might act as an immune modulator in some other way. Although these findings remain to be confirmed, especially in areas where iodine intake is lower, combined thyroxine and antithyroid-drug therapy may represent an advance in the quest for a regimen that is associated with a high rate of prolonged remission.

β -Adrenergic-Antagonist Drugs

β -Adrenergic-antagonist drugs are useful adjunctive agents in patients with Graves' **hyperthyroidism**, in that they ameliorate some of the symptoms and signs of the disease, such as tremor, anxiety, and palpitations, more rapidly than does antithyroid-drug therapy. They need not be given unless symptoms are moderate or severe, and should be discontinued as the patient becomes euthyroid. These drugs do not affect the synthesis and secretion of thyroid hormones and therefore should not be used alone except for short periods before radioiodine or surgical therapy. Despite their different pharmacologic characteristics, propranolol, metoprolol, atenolol, and nadolol are all effective in patients with **hyperthyroidism**^{37,38,39}. Compliance may be improved by using nadolol (80 mg a day) or atenolol (50 to 100 mg a day), because these drugs can be given only once a day. Caution must be exercised in treating patients with asthma or heart failure, even if it is related to **hyperthyroidism**.

Inorganic Iodide

Iodine given in pharmacologic doses (as Lugol's solution or as a saturated solution of potassium iodide) inhibits the release of thyroid hormones for a few days or weeks, after which its antithyroid action is lost⁴⁰. For this reason it is not used routinely, but short-term iodine therapy is useful in the preparation of patients for surgery (see below), after radioiodine therapy to hasten the fall in serum thyroxine and triiodothyronine concentrations to normal (although this is not a routine indication), and in the treatment of thyrotoxic crisis

(thyroid storm; see below). The usual dose of Lugol's solution (5 percent iodine and 10 percent potassium iodide in water) is 0.1 to 0.3 ml three times daily, and that of potassium iodide is 60 mg (one drop) three times daily.

Radioiodine Therapy

Indications and Regimens

Radioiodine is increasingly used as first-line therapy for Graves' **hyperthyroidism** and is the treatment of choice for recurrent **hyperthyroidism** after antithyroid-drug therapy. The objective of radioiodine therapy is to destroy sufficient thyroid tissue to cure **hyperthyroidism**. The goal of treatment may be to render the patient either euthyroid or hypothyroid, depending on the willingness of the physician to risk the possibility of persistent **hyperthyroidism**.

Much attention has focused on achieving euthyroidism by adjusting the dose of radioiodine, but there is little consensus regarding the most appropriate dose schedule. The regimens used include repeated low doses (2 mCi), fixed doses of 5 or 10 mCi, and doses calculated on the basis of the size of the thyroid, the uptake of radioiodine, or the turnover of iodine-131^{41,42,43,44,45,46,47}. There is no evidence that giving a calculated dose of radioiodine has any advantage over a fixed dose of 5 or 10 mCi,⁴⁸ and calculated doses have the disadvantages of inconvenience (more than one hospital visit is required because of the need to measure radioiodine uptake) and higher cost. Measurement of thyroid uptake of a tracer dose of iodine-131 is not a prerequisite for radioiodine treatment if the patient has Graves' disease (or toxic multinodular goiter).

A common approach to Graves' **hyperthyroidism** is to administer a single dose of 5 or 10 mCi. If the **hyperthyroidism** is not cured, a similar or larger dose should be given in six months; additional doses are rarely needed. Some physicians prefer to administer a single larger dose (15 mCi) initially with the intent of inducing hypothyroidism in most patients⁴⁹; the disadvantage of this approach is that patients will need to be treated with thyroxine, with the attendant risk of decreased bone mineral density and the possible risk of osteoporotic fractures if they receive too much, and the risk of hypercholesterolemia and possible ischemic heart disease if they receive too little^{50,51,52,53}. The imposition of stringent safety restrictions (especially outside the United States) in terms of returning to work and being in contact with children (in the United Kingdom it is recommended that a nursery-school teacher given 15 mCi of radioiodine stay out of work for three weeks) has made the use of lower doses more convenient.

Post-Treatment Thyroid Function

Radioiodine therapy cures **hyperthyroidism** and decreases the size of the thyroid in virtually all patients given multiple doses or a single large dose^{41,42}. Once euthyroidism has been achieved, **hyperthyroidism** rarely recurs^{54,55}. Hypothyroidism occurring within the first six months after treatment may be transient or permanent⁵⁶; if a patient with mild hypothyroidism is treated with thyroxine, later withdrawal of treatment and reassessment of the need for continuing therapy are indicated. Permanent hypothyroidism is the only

important complication of radioiodine therapy, occurring in at least 50 percent of patients given high doses by 1 year⁴⁹ and in at least 50 percent of those given lower doses by 25 years (Figure 2)⁴¹. It is dose-dependent, and its incidence remains at 2 to 3 percent per year many years after therapy^{41,57}. Hypothyroidism is likely if the serum thyrotropin concentration is elevated and the serum free thyroxine concentration is normal (subclinical hypothyroidism)⁵⁸. Long-term follow-up is essential.

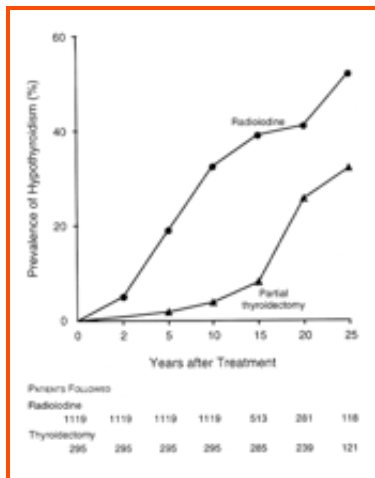


Figure 2. Prevalence of Hypothyroidism after Treatment with Radioiodine Therapy or after Partial Thyroidectomy.

The numbers of patients followed at each time point are shown below the figure. Adapted from Franklyn et al.⁴¹ with the permission of the publisher.

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Other Side Effects and Adjunctive Treatment

Patients treated with radioiodine are often also treated with an antithyroid drug or a β -adrenergic-antagonist drug. Young patients and patients with mild **hyperthyroidism** may be given radioiodine as the sole treatment, although often euthyroidism will not be achieved for several months. This slow response and the low risk of arrhythmias and angina in elderly patients and patients with severe **hyperthyroidism** make pretreatment for several weeks with an antithyroid drug or β -adrenergic-antagonist drug advisable in most patients. The standard practice is to withdraw the antithyroid drug three or four days before radioiodine therapy and resume it three or four days after therapy. It is uncertain whether administering an antithyroid drug before and after radioiodine treatment affects the response to this therapy, although in one study, starting antithyroid-drug treatment within eight days after radioiodine therapy resulted in a lower rate of hypothyroidism and a higher rate of persistent **hyperthyroidism**⁵⁹. Aside from hypothyroidism, radioiodine has few adverse effects. Occasionally there is transient worsening of **hyperthyroidism** within the first two weeks after radioiodine therapy. This is caused by radiation thyroiditis, which may also cause thyroid pain, tenderness, and swelling. Radiation thyroiditis severe enough to cause thyrotoxic crisis is very rare.

Ophthalmopathy

A subject of continuing debate in the treatment of patients with Graves' **hyperthyroidism** is the effect of the

different antithyroid treatments on ophthalmopathy. A large retrospective study revealed no difference in the development or worsening of ophthalmopathy in patients treated with an antithyroid drug alone, partial thyroidectomy, or radioiodine⁶⁰. In contrast, in a recent study of patients more than 35 years old who were randomly assigned to treatment with methimazole, surgery, or radioiodine, the frequency of development or worsening of eye disease was higher among those treated with radioiodine⁶¹. Explanations for the greater effect of radioiodine include the development of hypothyroidism and the release of thyroid antigens due to radiation thyroiditis. Ophthalmopathy was associated with a higher serum concentration of triiodothyronine before treatment,⁶¹ which accords with the clinical impression that ophthalmopathy is more often a problem in patients whose **hyperthyroidism** is difficult to control. We avoid giving radioiodine to patients with active and progressive ophthalmopathy, giving them an antithyroid drug instead until their eye disease becomes stable.

Cancer and Teratogenesis

Although thyroid cancer has been described in occasional patients treated with radioiodine,⁶² no relation was found between radioiodine and thyroid cancer in several large studies⁶³. There is similarly no evidence of an increase in the rate of leukemia or solid tumors except gastric cancer, the risk of which rises 10 years or more after treatment (when the standardized incidence ratio is 1.33), and breast cancer, the risk of which rises (though not significantly) after 30 years^{64,65,66}.

Less direct information is available about radioiodine and the risks of congenital abnormality. Pregnancy is an absolute contraindication to radioiodine therapy; therapy given inadvertently after the fetal thyroid has developed (by 10 weeks of gestation) is associated with ablation of the gland and therefore congenital hypothyroidism⁶⁷. Women of reproductive age should be given radioiodine within 10 days after the onset of menses or, if their cycles are irregular, after a negative pregnancy test, and they should avoid becoming pregnant for four months. There is no evidence of an increase in the rate of congenital abnormalities among the offspring of women treated with radioiodine⁶⁸. The theoretical risk of genetic abnormality resulting from radioiodine treatment in women and men has been estimated to be 0.005 percent,⁶⁹ and not surprisingly, such a risk has not been demonstrated in clinical studies.

Subtotal Thyroidectomy

Among patients with Graves' **hyperthyroidism**, subtotal thyroidectomy is appropriate treatment only for those who refuse radioiodine therapy and for the few with large goiters who have symptoms of compression or cosmetic concerns.

Preparation and Adverse Effects

Any patient with **hyperthyroidism** scheduled to undergo surgery should be treated with methimazole until he or she is euthyroid. Alternative methods of preoperative therapy include methimazole combined with potassium iodide (60 mg three times a day for 10 days), short-term therapy with propranolol alone⁷⁰ (or a

longer-acting β -adrenergic antagonist), or potassium iodide (for 10 days) in combination with propranolol⁷¹. Any of these regimens reduces the risk of postoperative thyrotoxic crisis virtually to zero.

Damage to the recurrent laryngeal nerve, hypoparathyroidism, and bleeding into the neck are recognized but uncommon adverse effects of subtotal thyroidectomy. The mortality rate for elective surgery is close to zero, and the rate of complications is reported to be less than 4 percent⁷².

Postoperative Thyroid Function

Relapse of **hyperthyroidism** occurs in at least 10 percent of patients, most often during the first 5 years after surgery, but at least 40 percent of relapses occur later, some as long as 30 years later⁷³. The reported rates of hypothyroidism are difficult to interpret because of the need to differentiate short-term from long-term hypothyroidism. At least one third of patients have a transient increase in the serum thyrotropin level three months after surgery⁷⁴. Patients with an elevated serum thyrotropin level but a normal serum thyroxine concentration (subclinical hypothyroidism) within the first year after surgery should not be considered to have permanent hypothyroidism. If thyroxine therapy is given, it should be withdrawn after one year and thyroid function reassessed. Permanent hypothyroidism occurs in 5 percent of patients within the first year, and thereafter in one or two patients per year, so that up to 50 percent of patients are hypothyroid by 25 years⁴¹ or earlier⁷⁵ ([Figure 2](#)). The proportion is even higher if patients with subclinical hypothyroidism are included.

Management of Toxic Adenoma or Toxic Nodular Goiter

A toxic thyroid adenoma or toxic multinodular goiter may be suspected as the cause of **hyperthyroidism** in any patient with no ophthalmopathy or diffuse goiter, especially if the patient is middle-aged or elderly¹⁰. The diagnosis is based primarily on physical examination and is confirmed by a radionuclide scan that shows uptake into a single thyroid nodule or patchy uptake into more than one hyperfunctioning nodule.

Hyperthyroidism due to thyroid nodular disease is permanent; there are no spontaneous remissions. Antithyroid-drug therapy, therefore, even though it may decrease thyroid hormone secretion, is not appropriate long-term therapy. A β -adrenergic-antagonist drug is useful, as in Graves' **hyperthyroidism**. Up to 40 percent of patients over the age of 60 have atrial fibrillation⁷⁶; they should be treated with warfarin to prevent embolic complications, although its efficacy has not been established⁷⁷.

The most appropriate treatment for **hyperthyroidism** caused by thyroid nodular disease is radioiodine. Whether the cause is a toxic nodular goiter or a single toxic adenoma, larger doses may be required to induce euthyroidism than in Graves' disease. The recommended dose ranges from 10 to 50 mCi^{78,79,80}. It is better to give more than less in order to minimize the risk of persistent **hyperthyroidism** in these patients, who tend to be elderly and have prominent cardiovascular manifestations of **hyperthyroidism**. The reported incidence of hypothyroidism varies; some studies suggest that these patients rarely become hypothyroid,⁸¹ whereas others report that hypothyroidism occurs among them as often as among patients with Graves'

disease⁸². The size of the thyroid adenoma or multinodular goiter should decrease after radioiodine therapy. Surgical treatment is indicated only if the patient refuses radioiodine treatment or has a very large multinodular goiter.

Management of Hyperthyroidism Caused by Thyroiditis

Among patients with **hyperthyroidism**, subacute thyroiditis should be suspected if the patient has pain and tenderness in the thyroid region, whereas silent thyroiditis should be suspected if the patient has been hyperthyroid only a few weeks, has little or no goiter, and has no extrathyroidal manifestations of Graves' disease. The latter constellation also characterizes postpartum thyroiditis, which occurs within the first six months after delivery¹¹. In patients with any form of thyroiditis, **hyperthyroidism** results from unregulated, inflammation-induced release of stored thyroxine and triiodothyronine. Radioiodine uptake into the thyroid is low, and treatment with either an antithyroid drug or radioiodine is contraindicated because neither can work.

Hyperthyroidism associated with thyroiditis usually is mild and lasts only a few weeks, and either no treatment or treatment with a β -adrenergic-antagonist drug is sufficient. In patients with subacute thyroiditis, short-term salicylate or even glucocorticoid therapy may be needed to relieve thyroid pain and tenderness. In patients with any type of thyroiditis, **hyperthyroidism** may be followed by hypothyroidism lasting one to four months, but thyroid function becomes normal in most patients. The hypothyroidism may be sufficiently symptomatic to warrant thyroxine therapy, which should be withdrawn after six months to determine whether treatment should be permanent. Among women who have postpartum thyroiditis, up to one third eventually become permanently hypothyroid^{11,83}.

Management of Hyperthyroidism in Pregnancy

Pregnant women with **hyperthyroidism** should be treated with an antithyroid drug. Both methimazole and propylthiouracil are effective; the drug chosen should be administered in the lowest possible dose to maintain the mother's serum thyroxine concentrations near the upper limit of the normal range since either drug can cross the placenta and cause goiter and hypothyroidism in the fetus. Combined treatment with methimazole and thyroxine is contraindicated because little of the thyroxine reaches the fetus and the mother must be given more methimazole if maternal **hyperthyroidism** is to be prevented. Propylthiouracil is the drug of choice for pregnant or lactating women because relatively little of it crosses the placenta, it appears in breast milk in only small amounts,⁸⁴ and it does not affect thyroid function in breast-feeding mothers⁸⁵. Furthermore, the rare congenital abnormality of aplasia cutis congenita may be associated with the use of methimazole in pregnancy.

Since Graves' disease tends to remit during pregnancy,⁸⁶ **hyperthyroidism** can usually be controlled with low doses of an antithyroid drug and it may be possible to discontinue therapy. Conversely, the disease tends to worsen or relapse after delivery⁸⁷.

Treatment of Thyrotoxic Crisis

Thyrotoxic crisis (thyroid storm), which may be defined as very severe clinical **hyperthyroidism** with marked tachycardia, fever, agitation, and weakness, is a medical emergency. In addition to supportive measures such as the administration of intravenous fluids and a glucocorticoid, an antithyroid drug should be administered (propylthiouracil given in a dose of 100 mg every six hours by mouth or nasogastric tube or rectally is preferable because of its ability to inhibit extrathyroidal conversion of thyroxine to triiodothyronine), as well as potassium iodide (by mouth or nasogastric tube or intravenously) to block the release of thyroid hormones. A β -adrenergic-antagonist drug should be given in a high dose (propranolol, 2 to 5 mg every four hours intravenously or 320 to 480 mg a day by mouth). The radiographic contrast agent ipodate sodium or iopanoic acid (1 g a day by mouth) can also be used. They inhibit the conversion of thyroxine to triiodothyronine, and the iodine released when these agents are metabolized has an antithyroid effect⁸⁸.

Summary

Although effective treatments for **hyperthyroidism** are available, none is perfect. Particularly with respect to Graves' disease, what is needed is a therapy directed at modulating the disease process itself rather than merely reducing the synthesis and secretion of thyroid hormones in the hope that the underlying Graves' disease will remit. Greater understanding of the pathogenesis of Graves' disease, resulting from cloning of the thyrotropin receptor⁸⁹ and better knowledge of the interactions between these receptors or other thyroid antigens and the immune system, may lead to such treatment. Broad-spectrum immunosuppression, with all its side effects, is not the answer; more focused therapies to inhibit the immune response to specific thyroid antigens may represent the treatment of the future. Meanwhile, radioiodine therapy is the most effective and convenient method of achieving long-term control of **hyperthyroidism**, although at the cost of hypothyroidism in many patients.

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