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Thyrotoxicosis and Thyroid Storm

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In the spectrum of endocrine emergencies, thyroid storm ranks as one of the most critical illnesses. Recognition and appropriate management of life-threatening thyrotoxicosis is vital to prevent the high morbidity and mortality that may accompany this disorder. The incidence of thyroid storm has been noted to be less than 10% of patients hospitalized for thyrotoxicosis; however, the mortality rate due to thyroid storm ranges from 20 to 30% [1,2].

In common parlance, whereas hyperthyroidism refers to disorders that result from overproduction of hormone from the thyroid gland, thyrotoxicosis refers to any cause of excessive thyroid hormone concentration. Thyroid storm represents the extreme manifestation of thyrotoxicosis [3]. The point at which thyrotoxicosis transforms to thyroid storm is controversial, and is, to some degree, subjective. In an effort to standardize and objectify thyroid storm somewhat, as compared with severe thyrotoxicosis, Burch and Wartofsky [4] have delineated a point system assessing degrees of dysfunction in various systems (thermoregulatory, central nervous, gastrointestinal, and cardiovascular), as shown in Table 1. However, clinically, it is prudent to assume that someone with severe thyrotoxicosis has impending thyroid storm, and to treat them aggressively, rather than focus on specific definitions.

Etiology

The most common underlying cause of thyrotoxicosis in cases of thyroid storm is Graves' disease. Graves' disease is mediated by the thyrotropin

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Table 1
Diagnostic criteria for thyroid storm

Diagnostic parameters	Scoring points
Thermoregulatory dysfunction	
Temperature	
99–99.9	5
100–100.9	10
101–101.9	15
102–102.9	20
103–103.9	25
$\geq$104.0	30
Central nervous system effects	
Absent	0
Mild (agitation)	10
Moderate (delirium, psychosis, extreme lethargy	20
Severe (seizures, coma)	30
Gastrointestinal-hepatic dysfunction	
Absent	0
Moderate (diarrhea, nausea/vomiting, abdominal pain)	10
Severe (unexplained jaundice)	20
Cardiovascular dysfunction	
Tachycardia (beats/minute)	
90–109	5
110–119	10
120–129	15
$\geq$140	25
Congestive heart failure	
Absent	0
Mild (pedal edema)	5
Moderate (bibasilar rales)	10
Severe (pulmonary edema)	15
Atrial fibrillation	
Absent	0
Present	10
Precipitating event	
Absent	0
Present	10

Scoring system: A score of 45 or greater is highly suggestive of thyroid storm; a score of 25–44 is suggestive of impending storm, and a score below 25 is unlikely to represent thyroid storm.

Adapted from Burch HB, Wartofsky L. Life-threatening thyrotoxicosis. Thyroid storm. Endocrinol Metab Clin North Am 1993;22(2):263–77.

receptor antibodies that stimulate excess and uncontrolled thyroidal synthesis and secretion of thyroid hormones (thyroxine [T_4] or triiodothyronine [T_3]). It occurs most frequently in young women, but can occur in either sex and any age group. However, thyroid storm can also occur with a solitary toxic adenoma or toxic multinodular goiter. Rare causes of thyrotoxicosis leading to thyroid storm would include hypersecretory thyroid

carcinoma, thyrotropin-secreting pituitary adenoma, struma ovarii/teratoma, and human chorionic gonadotropia–secreting hydatidiform mole. Other causes include interferon alpha and interleukin-2–induced thyrotoxicosis during treatment for other diseases, such as viral hepatitis and HIV infection [5–8]. Particularly relevant is hyperthyroidism aggravated by iodine exposure, which can occur, for example, following the intravenous administration of radiocontrast dye, or during or after amiodarone administration.

Given the background of hyperthyroidism due to the above causes, a precipitating event usually ignites the transition from thyrotoxicosis to thyroid storm. Thyroid storm can be precipitated by systemic insults such as surgery, trauma, myocardial infarction, pulmonary thromboembolism, diabetic ketoacidosis, parturition, or severe infection [5]. Thyroid storm has also been reported to be precipitated by the discontinuation of antithyroid drugs, excessive ingestion or intravenous administration of iodine (eg, radiocontrast dyes, amiodarone), radioiodine therapy, and even pseudoephedrine and salicylate use. Salicylates may increase free thyroid hormone levels disproportionately [9]. In the past, thyroid surgery in patients who had uncontrolled hyperthyroidism was the most common cause of thyroid storm. However, appropriate recognition and preparation before thyroid surgery has decreased, but not eliminated, the perioperative incidence of thyroid storm. The most common precipitating cause of thyroid storm currently seems to be infection, although it is difficult to know if published reports mirror actual frequencies [10].

To appreciate the pathogenesis of thyroid storm, one must first consider the mechanism of action of thyroid hormone at the nuclear level. Circulating, or free, T_4 and T_3 are taken into the cytoplasm of cells. T_4 is converted to its active form, T_3, by 5′-deiodinase enzyme(s). Conversion of T_4 to T_3 is accomplished by deiodination in the outer ring of the T_4 molecule. The three deiodinase proteins are D1, D2, and D3. Type I deiodinase (D1) and Type II deiodinase (D2) facilitate outer ring deiodination of T_4 to T_3. Normally, deiodination of T_4 to T_3 provides only 20% to 30% of T_3 (with the remaining emanating from direct thyroid secretion); however, it may provide more than 50% of T_3 in the thyrotoxic state. D1 is sensitive to inhibition by propylthiouracil, and D2 is insensitive to it. D1 activity has been noted in the liver, kidney, thyroid, and pituitary. D2 is responsible for most of the T_3 production in the euthyroid state. D2 mRNA is expressed in vascular smooth muscle, thyroid, heart, brain, spinal cord, skeletal muscle, and placenta. Type 3 deiodinase (D3) catalyzes the conversion of T_4 to reverse T_3 and to 3,3′–diiodothyronine (T2) which are both inactive. D3 is mainly present in the central nervous system, skin, and placenta [11].

After T_4 is deiodinated to T_3, it can then exert its effect by passing into the nucleus and binding to thyroid hormone receptors or thyroid hormone–responsive elements, to induce gene activation and transcription [4,12]. Thyroid hormone exerts its influence through nongenomic and genomic or nuclear effects. Nongenomic effects (eg, mitochondrial) usually occur

rapidly, whereas genomic effects require at least several hours to cause a modification of gene transcription. Thyroid hormone has specific effects in different tissues of the body. In the pituitary gland, T_3 exerts negative regulation on the transcription of the genes for the beta subunit and the common alpha subunit of thyrotropin, resulting in a suppressed thyrotropin in the context of thyrotoxicosis. Thyroid hormone also stimulates lipogenesis and lipolysis by inducing enzymes important early in the lipogenic pathway, including malic enzyme, glucose-6-phosphate dehydrogenase, and fatty acid synthetase. T_3 also accelerates the transcription of 3-hydroxy-3-methylglutaryl coenzyme A reductase. Although cholesterol production is increased, excretion of cholesterol in the bile is also accelerated, generally resulting in a decrease in total cholesterol. Thyroid hormone exerts its effect on bone by stimulating both osteogenesis and osteolysis, resulting in faster bone remodeling [12]. Thyroid hormone effects on the heart and cardiovascular system are many, resulting in decreased systemic vascular resistance, increased blood volume, increased contractility, and increased cardiac output [13].

One hypothesis to explain the cause of thyroid storm is an increase in the amount of free thyroid hormones. Of course, the elevated serum and intracellular levels of T_4/T_3 suppress thyrotropin, so that serum thyrotropin should be undetectable, except in very unusual cases (eg, pituitary thyrotropin-secreting adenoma). In one study comparing 6 subjects with thyroid storm to 15 subjects with more typical thyrotoxicosis, Brooks and colleagues [14] found that the mean free T_4 concentration was higher in subjects with thyroid storm, whereas the total T_4 concentration was similar in both groups. Another theory that may explain the pathogenesis of thyroid storm is a possible increase in target cell beta-adrenergic receptor density or postreceptor modifications in signaling pathways [4,15,16].

The important clinical point is that it is best to consider severe thyrotoxicosis or thyroid storm in ill patients and to approach and treat them in an active, preemptory fashion when possible. The distinction between severe thyrotoxicosis and life-threatening thyrotoxicosis, or thyroid storm, is a matter of clinical judgment. Although objective means such as the point scale by Burch and Wartofsky can, and perhaps should, be used, it is most prudent to treat a patient aggressively for his/her hyperthyroidism, rather than excessively contemplate whether this case really meets the criteria for thyroid storm. Close clinical monitoring is also required, usually in an intensive care unit. There is no arbitrary serum T_4 or T_3 cutoff that discriminates severe thyrotoxicosis from thyroid storm. Also, systemically ill patients have decreased ability to convert T_4 to T_3. Therefore, a minimally elevated T_3 or even a "normal" T_3 may be considered inappropriately elevated in the context of systemic illness.

Clinical presentation

The signs and symptoms of thyrotoxicosis are outlined in Table 2.

Table 2
Signs and symptoms of thyrotoxicosis

Organ system	Symptoms	Signs
Neuropsychiatric/Neuromuscular	Emotional lability	Muscle wasting
	Anxiety	Hyperreflexia
	Confusion	Fine tremor
	Coma	Periodic paralysis
Gastrointestinal	Hyperdefecation	
	Diarrhea	
Reproductive	Oligomenorrhea	Gynecomastia
	Decreased libido	Spider angiomas
Thyroid gland	Neck fullness	Diffuse enlargement
	Tenderness	Bruit
Cardiorespiratory	Palpitations	Atrial fibrillation
	Dyspnea	Sinus tachycardia
	Chest pain	Hyperdynamic precordium
		Congestive heart failure
Dermatologic	Hair loss	Pretibial myxedema
		Warm, moist skin
		Palmar erythema
Ophthalmologic	Diplopia	Exophthalmos
	Eye irritation	Ophthalmoplegia
		Conjunctival injection

Constitutional

One of the common findings in thyrotoxicosis is weight loss, despite having the same or greater caloric intake. The hypermetabolic state results in an imbalance of greater energy production compared with energy use, resulting in increased heat production and elimination. The thermogenesis leads to increased perspiration and heat intolerance. Other constitutional symptoms reported are generalized weakness and fatigue [17].

Neuropsychiatric

Neuropsychiatric manifestations of thyrotoxicosis include emotional lability, restlessness, anxiety, agitation, confusion, psychosis, and even coma [18]. In fact, behavioral studies reveal poor performance in memory and concentration testing proportional to the degree of thyrotoxicosis [17].

Gastrointestinal

Gastrointestinal symptoms include increased frequency of bowel movements due to increased motor contraction in the small bowel, leading to more rapid movement of intestinal contents.

Reproductive symptoms

Reproductive symptoms include changes in the menstrual cycle, including oligomenorrhea and anovulation. In men, symptoms can include decreased

libido, gynecomastia, and development of spider angiomas, perhaps related to an increase in sex hormone-binding globulin and a subsequent increase in estrogen activity [17].

Cardiorespiratory

Cardiorespiratory symptoms of thyrotoxicosis include palpitations and dyspnea on exertion. The shortness of breath can be multifactorial in origin because of decreased lung compliance, engorged pulmonary capillary bed, or left ventricular failure. Thyrotoxic patients may also experience chest pain similar to angina pectoris, owing to increased myocardial oxygen demand and coronary artery spasm, although coronary artery disease should be excluded as appropriate. Physical findings with thyroid storm can include a hyperdynamic precordium with tachycardia, increased pulse pressure, and a strong apical impulse. A pleuropericardial rub may also be heard occasionally, and there may be evidence of heart failure [17].

Thyroid

Thyroid gland findings can vary, depending on the cause of the thyrotoxicosis. With Graves' disease, diffuse enlargement of the gland, and possibly a bruit, can be appreciated, caused by increased vascularity and blood flow. Other potential accompanying signs in Graves' disease include inflammatory ophthalmopathy and, possibly, localized dermal myxedema. The myxedema associated with Graves' disease tends to occur in the pretibial areas and can appear as asymmetric, raised, firm, pink-to-purple brown plaques of nonpitting edema. With a toxic multinodular goiter, physical findings of the thyroid gland may include one or more nodules. With subacute thyroiditis, a tender thyroid gland could be found, and may be accompanied by constitutional complaints of fever and malaise [17,19].

In older individuals, typical symptoms of thyrotoxicosis may not be apparent. Older patients may present with "apathetic" thyrotoxicosis, with some atypical symptoms including weight loss, palpitations, weakness, dizziness, syncope, or memory loss, and physical findings of sinus tachycardia or atrial fibrillation [17].

Diagnosis

In thyroid storm, the pattern of elevated free T_4 and free T_3 with a depressed thyrotropin (less than 0.05 μU/mL) can be comparable to the levels seen in thyrotoxicosis. After synthesis of thyroid hormone, the thyroid gland secretes mainly T_4. Approximately 80% of circulating T_3 is derived from monodeiodination of T_4 in peripheral tissues, whereas only about 20% emanates from direct thyroidal secretion. Both T_4 and T_3 are then bound to proteins: thyroxine-binding globulin, transthyretin, and albumin. Only a small fraction of the hormones, 0.025% of T_4 and 0.35% of T_3, are free

and unbound [17,19]. Because the laboratory measurement of total T_3 and total T_4 measures mainly protein-bound hormone concentrations, results may be affected by conditions that affect protein binding. Thyroxine-binding globulin is elevated in infectious hepatitis and pregnancy, and in patients taking estrogens or opiates. In addition, many drugs interfere with protein binding, including heparin, furosemide, phenytoin, carbamazepine, diazepam, salicylates, and nonsteroidal anti-inflammatory drugs. Because of this interference with total thyroid hormone levels, free hormone concentrations are preferable in the diagnosis of thyrotoxicosis [9].

Serum total and free T_3 concentrations are elevated in most patients who have thyrotoxicosis because of increased thyroidal T_3 production and more rapid extrathyroidal conversion of T_4 to T_3. In less than 5% of patients who have thyrotoxicosis in North America, there can be an increase in serum-free T_3 while having a "normal" free T_4, referred to as "T_3 toxicosis" [17,19]. With Graves' disease and toxic nodular goiter, there tends to be a higher proportion of T_3, with a T_3/ T_4 ratio of greater than 20. With thyrotoxicosis caused by thyroiditis, iodine exposure, or exogenous levothyroxine intake, there is generally a greater proportion of T_4, with a T_3/ T_4 ratio of less than 15 [19].

Other possible laboratory findings associated with thyrotoxicosis include hyperglycemia, hypercalcemia, elevated alkaline phosphatase, leukocytosis, and elevated liver enzymes. The hyperglycemia tends to occur because of a catecholamine-induced inhibition of insulin release, and increased glycogenolysis. Mild hypercalcemia and elevated alkaline phosphatase can occur because of hemoconcentration and enhanced thyroid hormone–stimulated bone resorption [9,15,18,20].

Adrenocortical function is also affected by thyrotoxicosis. Thyrotoxicosis accelerates the metabolism of endogenous or exogenous cortisol by stimulating the rate-limiting step in the degradation of glucocorticoids, which is accomplished by the hepatic enzymes, Δ4,5 steroid reductases. Therefore, cortisol and other steroids, including corticosterone, deoxycorticosterone, and aldosterone are metabolized at an accelerated rate [21]. However, with thyrotoxicosis, both degradation and production of cortisol should be accelerated, resulting in a normal to increased circulating cortisol level. Given the stressful condition of thyroid storm, a normal cortisol level may be interpreted as an indication of some degree of adrenal insufficiency. Objectively, basal serum cortisol and cortisol responses to a corticotropin stimulation test should be normal. However, it has been found that adrenocortical reserve in long-standing, severe thyrotoxicosis can be diminished [21]. Tsatsoulis and colleagues [22] assessed adrenocortical reserve in 10 subjects with severe, long-standing (4–6 months) thyrotoxicosis with a low-dose corticotropin stimulation test following dexamethasone pretreatment. The subjects were tested while they were thyrotoxic before treatment, and again after treatment, once they had become euthyroid. The cortisol response to the corticotropin stimulation test decreased significantly when subjects

were thyrotoxic, compared with the cortisol response in the euthyroid state, perhaps indicating a relative adrenal insufficiency [10,22]. Interpretation of corticotropin stimulation tests in the context of serious illnesses is an important issue, but beyond the scope of this article.

Radiologic imaging is not required to make the diagnosis of thyrotoxicosis or thyroid storm. However, in the evaluation of thyroid storm, a chest radiograph (or chest CT without contrast when appropriate) would be helpful to seek a possible infectious source as a precipitant. Although not always indicated for diagnosis, given the urgency and clinical context, nuclear medicine imaging with radioactive iodine uptake and scanning would reveal a greatly increased uptake of radioiodine as early as 1 or 2 hours after administration of the isotope, indicating rapid intraglandular turnover of iodine [15]. It is frequently helpful, and generally easier in the setting of an intensive care unit, to obtain a thyroid sonogram with Doppler flow to assess thyroid gland size, vascularity, and the presence of nodules that may require further attention. Typically, a thyroid gland secreting excessive hormones would be enlarged and have enhanced Doppler flow. On the other hand, in the setting of subacute, postpartum, or silent thyroiditis, or exogenous causes of hyperthyroidism, the thyroid gland would be expected to be small, with decreased Doppler flow.

Electrocardiogram manifestations of thyrotoxicosis most commonly include sinus tachycardia and atrial fibrillation. Sinus tachycardia occurs in approximately 40% of cases, whereas atrial fibrillation occurs in 10% to 20% of patients who have thyrotoxicosis, with a tendency to occur more commonly in patients older than 60, who are more likely to have underlying structural heart disease [23]. The extent of evaluation before therapy depends on the urgency of the clinical condition, and additional studies can be obtained once antithyroid therapy is initiated.

Management

The medical management of thyroid storm consists of an array of medications that act to halt the synthesis, release, and peripheral effects of thyroid hormone. Management of thyroid storm is outlined in Table 3. This multidrug approach has proven to be vitally important in the expeditious control of life-threatening thyrotoxicosis. This therapeutic armamentarium has multiple targets: stopping synthesis of new hormone within the thyroid gland; halting the release of stored thyroid hormone from the thyroid gland; preventing conversion of T_4 to T_3; controlling the adrenergic symptoms associated with thyrotoxicosis; and controlling systemic decompensation with supportive therapy [5,18].

The order of therapy in treating thyroid storm is very important, with regard to use of thionamide therapy and iodine therapy. In most patients, inhibition of thyroid gland synthesis of new thyroid hormone with a thionamide should be initiated before iodine therapy, to prevent the

Table 3
Management of thyroid storm

Medication	Dosage	Mechanism of action	Conditions of use
I. Inhibition of new hormone production			
Propylthiouracil	200–400 mg po q 6–8 h[a]	Inhibits new hormone synthesis; decreases T4-to-T3 conversion	First-line therapy
or			
Methimazole	20–25 mg po q 6 h[a]	Inhibits new hormone synthesis	First-line therapy
II. Inhibition of thyroid hormone release			
Potassium iodide[b] SSKI	5 drops po q 6 h	Blocks release of hormone from gland	Administer at least 1 hr after thionamide
Lugol's solution[b]	4–8 drops po q 6–8 h	Blocks release of hormone from gland	Administer at least 1 hr after thionamide
Sodium ipodate[c] (308 mg iodine/ 500 mg tab)	1–3 g po qd	Blocks release of hormone from gland; inhibits T4-to-T3 conversion	Administer at least 1 h after thionamide
Iopanoic acid[c]	1 g po q 8 h for 24 h, then 500 mg po q 12 h	Blocks release of hormone from gland; inhibits T4-to-T3 conversion	Administer at least 1 h after thionamide
III. Beta-adrenergic blockade			
Propranolol	60–80 mg po q 4 h or 80–120 mg q 6 h	Beta-adrenergic blockade; decreases T4-to-T3 conversion	
Cardioselective agents:			
Atenolol	50–200 mg po qd	Beta-adrenergic blockade	Use when cardioselective agents preferred
Metoprolol	100–200 mg po qd		
Nadolol	40–80 mg po qd		
Intravenous agent:			
Esmolol	50–100 μg/kg/min	Beta-adrenergic blockade	Use when oral agents contraindicated; Consider use in heart failure

(*continued on next page*)

Table 3 (*continued*)

Medication	Dosage	Mechanism of action	Conditions of use
IV. Supportive treatment			
Acetaminophen	325–650 po/pr q 4–6 h as needed	Treatment of hyperthermia	Preferred treatment over salicylates
Hydrocortisone	100 mg IV q 8 h	Decreases T4-to-T3 conversion; vasomotor stability	Use when patient hypotensive to treat possible concomitant adrenal insufficiency
V. Alternative Therapies			
Lithium carbonate	300 mg po q 8 h[d]	Blocks release of hormone from gland; inhibits new hormone synthesis	Used when thionamide or iodide therapy is contraindicated; lithium levels should be checked regularly
Potassium perchlorate	1 g po qd	Inhibits iodide uptake by thyroid gland	Used in combination with thionamide in treatment of Type II amiodarone-induced thyrotoxicosis
Cholestyramine	4 g po qid	Decreases reabsorption of thyroid hormone from enterohepatic circulation	Used in combination with thionamide therapy

[a] Rectal formulations are described in article.

[b] SSKI (1 g/mL) contains 76.4% iodine. Five drops four times a day (assuming 20 drops/mL) contain about 764 mg iodine. Lugol's solution (125 mg/mL of total iodine) contains, in each 100 mL, 5 g of iodine and 10 g of potassium iodide. Four drops four times a day contain about 134 mg of iodine [40].

[c] These agents are no longer commercially available.

[d] Lithium dose should be adjusted to achieve serum concentration of 0.6–1.0 meq/L.

stimulation of new thyroid hormone synthesis that can occur if iodine is given initially [4,5,18]. However, the time delay between antithyroid agents administration and iodine administration is a matter of controversy, and can be only 30 to 60 minutes, depending on the clinical urgency.

Antithyroid drug therapy with thionamides has been used for treatment of thyrotoxicosis since the introduction of this class of medicine in 1943. The two specific antithyroid agent classes are thiouracils and imidazoles. Propylthiouracil is a thiouracil, whereas methimazole and carbimazole are imidazoles. Although propylthiouracil and methimazole are used widely in

the United States, carbimazole is not available in the United States, and is more commonly used in Europe. Carbimazole is metabolized rapidly to methimazole [24,25].

Within the thyroid gland, the thionamides interfere with the thyroperoxidase-catalyzed coupling process by which iodotyrosine residues are combined to form T_4 and T_3. Thionamides may also have an inhibitory effect on thyroid follicular cell function and growth [24]. Outside the thyroid gland, propylthiouracil, but not methimazole, inhibits conversion of T_4 to T_3. Thionamides may also have clinically important immunosuppressive effects, including decreasing antithyrotropin-receptor antibodies over time, and decreasing other immunologically important molecules, such as intracellular adhesion molecule 1 and soluble interleukin-2. Antithyroid drugs may also induce apoptosis of intrathyroidal lymphocytes and decrease HLA antigen class II expression [26].

Methimazole has a longer half-life than propylthiouracil, permitting less frequent dosing [27]. Although methimazole is free in the serum, 80%–90% of propylthiouracil is bound to albumin [24,26]. Either agent may be used to treat thyroid storm. Propylthiouracil has the additional theoretical advantage of inhibiting peripheral conversion of T_4 to T_3. On the other hand, the duration of action of methimazole is longer, such that it can be administered less frequently, as compared with three to four times daily for propylthiouracil (PTU). The authors recommend that the dosing in thyroid storm for propylthiouracil be 800 to 1200 mg daily in divided doses of 200 mg or 300 mg every 6 hours. The dosing for methimazole is 80 to 100 mg daily in divided doses of 20 to 25 mg every 6 hours (although once stable, the frequency of dosing can be decreased to once or twice daily) [18]. Typically, administration has been by mouth; however, both methimazole and propylthiouracil can be administered rectally [28–31]. Given that methimazole was shown to have similar pharmacokinetics for both oral and intravenous use in normal subjects and in subjects with hyperthyroidism, the parenteral route for methimazole should also be considered [32]. Although there are no commercially available parenteral formulations of the thionamides, there are case reports of methimazole being administered intravenously in circumstances where the oral and rectal route of administration could not be used [33,34].

The rectal formulations of the antithyroid drugs have been either as enemas or suppositories. Nabil and colleagues [28] used a suppository formulation of methimazole, in which 1200 mg of methimazole was dissolved in 12 mL of water with two drops of Span 80, mixed with 52 mL of cocoa butter. Yeung and colleagues [29] used an enema preparation of propylthiouracil, in which 12 50 mg tablets of propylthiouracil were dissolved in 90 mL of sterile water and administered by foley catheter inserted into the rectum, with the balloon inflated to prevent leakage. Walter and colleagues [30] used an enema formulation of propylthiouracil, composed of eight 50 mg tablets dissolved in 60 mL of Fleet's mineral oil or in 60 mL of Fleet's phospho soda. Jongjaroenprasert and colleagues [31] compared the use of an enema preparation of

propylthiouracil with a suppository preparation, assessing bioavailability and effectiveness. For the enema preparation, eight 50 mg tablets of propylthiouracil were dissolved in 90 mL of sterile water. For the suppository formulation, 200 mg of propylthiouracil were dissolved in a polyethylene glycol base and put into suppository tablets. The enema form provided better bioavailability than the suppository form. However, both preparations proved to have comparable therapeutic effect. Hodak and colleagues [33] prepared the intravenous preparation of methimazole by reconstituting 500 mg of methimazole powder with 0.9% sodium chloride solution to a final volume of 50 mL. The solution of 10 mg/mL was then filtered through a 0.22-μm filter and subsequently administered as a slow, intravenous push over 2 minutes, followed by a saline flush. Routine pharmacologic sterility tests need to be performed as indicated by local regulations.

Common adverse side effects of the antithyroid drugs include an abnormal sense of taste, pruritus, urticaria, fever, and arthralgias. More rare and serious side effects are agranulocytosis, hepatotoxicity, and vasculitis. With a criterion of absolute granulocyte count of less than 500 per cubic millimeter, 0.37% of subjects receiving propylthiouracil and 0.35% of subjects receiving methimazole developed agranulocytosis, in a large case series [35]. Most cases of agranulocytosis occur within the first 3 months of treatment, but can occur anytime after starting therapy. With methimazole, agranulocytosis tends to be dose-related, with occurrence being rare at doses of less than 40 mg daily. However, agranulocytosis does not appear to be dose-related with propylthiouracil use [25,26]. Nonetheless, agranulocytosis can occur at any time with either medication, and close monitoring is mandatory.

The use of granulocyte colony-stimulating factor (G-CSF) for treatment of agranulocytosis induced by antithyroid medications has been studied in a large retrospective study and a prospective controlled study. In the prospective study, Fukata and colleagues [36] showed that the use of G-CSF did not shorten recovery time in the treated, compared with the untreated, groups with moderate or severe agranulocytosis. In the retrospective study, Tajiri and colleagues [37,38] showed that G-CSF therapy did shorten recovery time in patients with antithyroid drug–induced agranulocytosis, as long as the absolute granulocyte count was above $0.1 \times 10(9)/L$. Therefore, the use of G-CSF can be recommended for treatment of antithyroid drug–induced agranulocytosis, with consideration of the individual context [26].

Hepatotoxicity can also occur in 0.1% to 0.2% of patients using antithyroid drugs. Hepatotoxicity related to propylthiouracil tends to be an allergic hepatitis with evidence of hepatocellular injury, whereas hepatotoxicity related to methimazole tends to result in hepatic abnormalities typical of a cholestatic process [26]. Vasculitis may also occur with antithyroid drug use, associated more commonly with propylthiouracil than with methimazole. This toxic antithyroid drug reaction is associated with some serologic markers: most patients have perinuclear antineutrophil cytoplasmic antibodies and antimyeloperoxidase antineutrophil cytoplasmic antibodies.

Some patients develop antineutrophil cytoplasmic antibody–positivity, which is associated with acute renal insufficiency, arthritis, skin ulcerations, vasculitic rash, and possibly sinusitis or hemoptysis [26].

In the setting of thyroid storm, iodine therapy complements the effects of thionamide therapy. Thionamide therapy decreases the synthesis of new hormone production; iodine therapy blocks the release of prestored hormone, and decreases iodide transport and oxidation in follicular cells. This decrease in organification due to increasing doses of inorganic iodide is known as the ''Wolff-Chaikoff'' effect. Small increments in available iodide cause increased formation of thyroid hormone; however, large amounts of exogenous iodide actually inhibit hormone formation. At iodide concentrations greater than 1 μmol/L, iodination is inhibited. However, despite maintenance of high doses of iodide, the thyroid gland eventually escapes this inhibition after approximately 48 hours. This escape occurs as the iodide transport system adapts to the higher concentration of iodide by modulating the activity of the sodium-iodide symporter [39]. Although iodide is effective at rapidly reducing serum thyroid hormone levels, usually within 7 to 14 days, most patients escape the inhibition and return to hyperthyroidism within 2 to 3 weeks, if no other treatment is given. Therefore, the use of iodide to treat thyrotoxicosis is of limited use, and thus is used only in severe thyrotoxicosis or thyroid storm in combination with thionamide therapy [40].

Administering iodine therapy before thionamide therapy affects short-term and longer-term treatment options for thyrotoxicosis. In the acute setting, if iodine therapy is given before thionamide therapy, new hormone synthesis can be stimulated. When planning definitive therapy for thyrotoxicosis after the acute phase of thyroid storm, use of exogenous iodine at any time can predispose a patient to increased surgical risk because of the enrichment of thyroid hormone stores, and can cause postponement of radioiodine ablation until an adequate clearance of the iodine load occurs [4]. Initial blockade of iodine organification begins within 1 hour of treatment with thionamide therapy. Therefore, to block the release of preformed thyroid hormone safely, iodine therapy should be administered no sooner than 30 to 60 minutes after thionamide therapy [5]. The biphasic effects of iodine are important and can be summarized. Over a short term of 1 to 3 weeks, iodine inhibits thyroid hormone synthesis and can be used as an effective antithyroid agent, especially in conjunction with propylthiouracil or methimazole. In all patients, but especially in those who are not also receiving propylthiouracil or methimazole, there may be escape from the Wolff-Chaikoff effect after 2 to 3 weeks of iodine administration, and exacerbation of hyperthyroidism may ensue. The chance of this latter hyperthyroid phase occurring is decreased, but not eliminated, by the adjunctive administration of propylthiouracil or methimazole.

Oral formulations of inorganic iodine include Lugol's solution and saturated solution of potassium iodide. The dosing for these preparations in

thyroid storm is 0.2 to 2 g daily, with four to eight drops of Lugol's solution (assuming 20 drops/mL, 8 mg iodine/drop) every 6 to 8 hours and five drops of saturation solution of potassium iodide (with 20 drops/mL, 38 mg iodide/drop) every 6 hours [4,40]. Parenteral sources of iodine, including sodium iodide, are no longer available in the United States. The oral iodinated contrast agents, iopanoic acid and sodium ipodate, have multiple effects on thyroid hormone in the periphery and within the thyroid gland. These iodinated contrast agents competitively inhibit Types 1 and 2 5′-monodeiodinase in the liver, brain, and thyroid, blocking conversion of T_4 to T_3, resulting in a rapid decrease in T_3 and an increase in reverse T_3. These iodinated contrast agents have also been found to inhibit binding of T_3 and T_4 to cellular receptors [10,18]. In thyroid storm, sodium ipodate (308 mg iodine/500mg capsule) is dosed at 1 to 3 g daily. Usually, iopanoic acid is dosed at 1g every 8 hours for the first 24 hours, followed by 500 mg twice daily [4,41]. Unfortunately, however, these very effective antithyroid agents are no longer marketed commercially or available.

Controlling the cardiovascular manifestations of thyrotoxicosis is a vital part of management. The cardiovascular changes seen with thyrotoxicosis occur because of the different effects of thyroid hormone on the heart and on systemic vasculature. Thyroid hormone decreases systemic vascular resistance by a direct vasodilatory action on smooth muscle and by endothelial release of nitric oxide or other endothelial-derived vasodilators. In response to thyroid hormone administration in hypothyroid patients, systemic vascular resistance may decrease by as much as 50% to 70% [42]. The decreased systemic vascular resistance leads to increased blood flow to the heart and other organs.

The effect of thyroid hormone on the heart is mediated partly by the genomic effects of T_3 binding to specific nuclear receptors. This binding activates thyroid hormone response elements within promoter enhancer regions of certain genes, which are partly responsible for modulating cardiac structure and contractility. Specifically, T_3 activates transcription of the α-myosin heavy chain (MHC-α) and represses transcription of the β-myosin heavy chain (MHC-β). Myofibrillar proteins, which compose the thick filaments of the cardiac myocyte, are made up of MHC-αs or MHC-βs. Three myosin isoforms have been identified in ventricular muscle: V1, made of MHC-α/α; V2, made of MHC-α/β; and V3, made of MHC-β/β. Thyroid hormone increases the synthesis of V1 and decreases the synthesis of V2, resulting in an increase in the velocity of muscle fiber shortening, because V1 has higher ATPase enzymatic activity [43].

T_3 also regulates production of the sarcoplasmic reticulum proteins, calcium-activated ATPase, phospholamban, and various plasma-membrane ion transporters through transcriptional and posttranscriptional effects. In addition to these genomic effects of T_3 in the heart, thyroid hormone also has nongenomic actions, directly altering the performance of sodium, potassium, and calcium channels [13,42].

Beta-blockade is essential in controlling the peripheral actions of thyroid hormone. The use of a beta-adrenergic receptor antagonist in the management of thyrotoxic crisis was first reported in 1966 with the agent pronethalol [44]. Soon thereafter, propranolol became the most commonly used beta-blocker in the United States [18]. In thyroid storm, propranolol is dosed at 60 to 80 mg every 4 hours, or 80 to 120 mg every 4 hours. The onset of action after oral dosing takes place within 1 hour. For a more rapid effect, propranolol can also be administered parenterally, with a bolus of 0.5 to 1 mg over 10 minutes followed by 1 to 3 mg over 10 minutes, every few hours, depending on the clinical context [15,41]. Esmolol can also be administered parenterally at a dose of 50 to 100 μg/kg/min [24]. Relatively large doses of propranolol are required in the setting of thyrotoxicosis because of the faster metabolism of the drug, and possibly because of a greater quantity of cardiac beta-adrenergic receptors [42].

Intravenous administration of beta-blockers should be performed in a monitored setting. In addition to its effect on beta-adrenergic receptors, propranolol in large doses (greater than 160 mg daily) can decrease T_3 levels by as much as 30%. This effect, mediated by the inhibition of 5′monodeiodinase, is mediated slowly over 7 to 10 days. Because propranolol has a short half-life and an increased requirement during thyrotoxicosis, multiple large daily doses are required. Longer-acting cardioselective beta-adrenergic receptor antagonists may be used also, and would require less frequent dosing. Atenolol can be used in thyrotoxicosis, with doses ranging from 50 to 200 mg daily, but may require twice daily dosing to achieve adequate control [25]. Other oral agents that can be used include metoprolol at 100 to 200 mg daily and nadolol at 40 to 80 mg daily [24]. The actual administered dose is determined by the clinical context, and modified as the clinical situation changes. Cardiovascular manifestations and responses should be monitored closely, with subsequent modulation of the dose of medication as appropriate.

Relative contraindications to beta-adrenergic receptor antagonist use include a history of moderate to severe heart failure or the presence of reactive airway disease. With the latter, beta-1 selective receptor antagonists, such as metoprolol or atenolol, would be recommended but, again, the individual clinical context must be considered carefully [25]. Beta-blockade may result in hypotension in some patients who have heart failure and are being treated for thyrotoxicosis. Because the use of beta-adrenergic receptor antagonists can be beneficial in the treatment of thyrotoxicosis, careful consideration is required. If the cause of the heart failure were likely to be underlying tachycardia, beta-blockade would be particularly useful. However, in situations in which the cause of the heart failure cannot be ascertained easily, beta-blockade should only be administered with a short-acting drug, under close hemodynamic monitoring [42].

One of the significant cardiovascular complications of thyrotoxicosis is atrial fibrillation, occurring in 10% to 35% of cases [45]. The issue of anticoagulation in atrial fibrillation in the setting of thyrotoxicosis has been

controversial. Studies assessing the incidence of embolic events in thyrotoxic patients who have atrial fibrillation have yielded conflicting information regarding the incidence of embolism [46,47]. In the largest retrospective study, it appears that thyrotoxic patients who have atrial fibrillation are not at greater risk for embolic events, compared with age-matched patients who have atrial fibrillation due to other causes [47]. The standard risk factors for embolic events in atrial fibrillation, including increased age and underlying heart disease, apply to thyrotoxic patients. The Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy recommends that, in thyrotoxic patients who have atrial fibrillation, antithrombotic therapies should be selected based on the presence of stroke risk factors [48]. Therefore, standard therapy with warfarin or aspirin would be indicated, according to these guidelines. Thyrotoxic patients may require a lower maintenance dose of warfarin than euthyroid patients because of increased clearance of vitamin K–dependent clotting factors [43].

Glucocorticoids, including dexamethasone and hydrocortisone, have also been used in the treatment of thyroid storm because they have an inhibitory effect on peripheral conversion of T_4 to T_3. Therefore, glucocorticoids can be effective in reducing T_3 levels as adjunctive therapy. The clinical relevance of this minor effect is unknown. Also, glucocorticoids are used in thyroid storm to treat possible relative adrenal insufficiency. One study found inappropriately normal levels of serum cortisol in a series of subjects with thyroid storm. This study found improved survival in those subjects treated with glucorticoids [4,49]. In patients who have severe thyrotoxicosis, especially in conjunction with hypotension, treatment with glucocorticoids has become standard practice because of the possibility of relative adrenal insufficiency, or the possibility of undiagnosed Addison's disease or adrenal insufficiency [21]. Dosing of glucorticoids in thyroid storm can be with hydrocortisone 100 mg intravenously every 8 hours, with tapering as the signs of thyroid storm improve.

Alternative therapies

Several therapeutic agents used in the treatment of thyrotoxicosis are only considered when the first-line therapies of thionamides, iodide, beta-blockers, and glucocorticoids fail or cannot be used owing to toxicity. When iodide therapy cannot be used, another agent that can be used to inhibit thyroid hormone release is lithium. Lithium can be used when thionamide therapy is contraindicated because of toxicity or adverse reactions; it can also be used in combination with PTU or methimazole [50]. In summary, lithium has several effects on the thyroid gland, including directly decreasing thyroid hormone secretion and thereby increasing intrathyroidal iodine content, and inhibiting coupling of iodotyrosine residues that form iodothyronines (T_4 and T_3) [51–53]. In thyroid storm, the dosing for lithium is 300 mg every 8 hours [24]. To avoid lithium toxicity, lithium level should

be monitored regularly (perhaps even daily) to maintain a concentration of about 0.6–1.0 mEq/L [18,24]. Very frequent monitoring of serum lithium levels is mandatory, especially because the serum lithium concentrations may change as the patient is rendered more euthyroid.

Potassium perchlorate is another therapeutic agent used historically in the treatment of thyrotoxicosis. The perchlorate anion, ClO4-, is a competitive inhibitor of iodide transport [24]. However, its use fell out of favor for the treatment of thyrotoxicosis because of possible side effects of aplastic anemia and nephrotic syndrome. After thionamides became available, the risk of using potassium perchlorate outweighed its benefits. Recently, there has been a resurgence of interest in this agent, especially in selected patients who have amiodarone-induced thyrotoxicosis (AIT). For treatment of cardiac arrhythmias, amiodarone can cause hypothyroidism or hyperthyroidism. Hypothyroidism is more prevalent in high-iodine intake regions, and AIT is more prevalent in low-iodine intake areas. AIT has been classified into two categories: Type I and Type II. Type I AIT frequently occurs in individuals with underlying thyroid abnormalities, such as nodular goiter or latent autoimmunity. The pathogenesis of the thyrotoxicosis is presumed to be caused by iodine-induced accelerated thyroid hormone synthesis. Type II AIT is considered to be a form of destructive thyroiditis, induced by amiodarone. Glucocorticoids have been successful in treating Type II AIT, and the combination of potassium perchlorate and methimazole has been successful in the treatment of Type I AIT. The potassium perchlorate exerts its action by inhibiting iodide uptake by the thyroid gland while organification is inhibited by methimazole. The regimen of potassium perchlorate (1 g daily) and methimazole (30–50 mg daily) has been found to normalize thyroid hormone levels successfully, with an average duration of treatment of 4 weeks. With a limited treatment course of approximately 4 weeks, and a dose of potassium perchlorate that is no greater than 1 g daily, the adverse effects of aplastic anemia and nephrotic syndrome did not occur in several studies [54–56].

Before beta-adrenergic receptor antagonists were used to counteract the peripheral effects of thyroid hormone, the antiadrenergic agents, reserpine and guanethidine, were often used. Reserpine is an alkaloid agent that depletes catecholamine stores in sympathetic nerve terminals and the central nervous system. Guanethidine also inhibits the release of catecholamines. Side effects of these medications include hypotension and diarrhea. Reserpine can also have central nervous system depressant effects. Therefore, these agents would be indicated only in rare situations where beta-adrenergic receptor antagonists are contraindicated, and when there is no hypotension or evidence of central nervous system–associated mental status changes [4]. Dosing for guanethidine in thyroid storm is 30 to 40 mg orally every 6 hours, and for reserpine 2.5 to 5 mg intramuscularly every 4 hours [18].

Cholestyramine, an anion exchange resin, has also been used in the treatment of thyrotoxicosis, to help decrease reabsorption of thyroid hormone

from the enterohepatic circulation [57]. Thyroid hormone is metabolized mainly in the liver, where it is conjugated to glucuronides and sulfates. These conjugation products are then excreted in the bile. Free hormones are released in the intestine and finally reabsorbed, completing the enterohepatic circulation of thyroid hormone. In states of thyrotoxicosis, there is increased enterohepatic circulation of thyroid hormone. Cholestyramine therapy has been studied in the treatment of thyrotoxicosis as an adjunctive therapy to thionamides, and has been found to decrease thyroid hormone levels rapidly. In several trials, cholestyramine therapy, in combination with methimazole or propylthiouracil, caused a more rapid decline in thyroid hormone levels than standard therapy with thionamides alone. Cholestyramine was also found to be useful in rapidly decreasing thyroid hormone levels in a case of iatrogenic hyperthyroidism. In these trials, cholestyramine was dosed at 4 g orally four times a day [57–60]. The effect of cholestyramine is generally minimal and it should not be administered at the exact same time as other medications because it may inhibit their absorption. On the other hand, cholestyramine is not expected to be associated with significant adverse effects.

When clinical deterioration occurs in thyroid storm, despite the use of all of these medications, removal of thyroid hormone from circulation would be a therapeutic consideration. Plasmapheresis, charcoal hemoperfusion, resin hemoperfusion, and plasma exchange have been found to be effective in rapidly reducing thyroid hormone levels in thyroid storm [61–63].

Supportive care/treatment of precipitating cause

Supportive care is an important part of the multisystem therapeutic approach to thyroid storm. Because fever is very common with severe thyrotoxicosis, antipyretics should be used; acetaminophen is the preferable choice. Salicylates should be avoided in thyrotoxicosis because salicylates can decrease thyroid protein binding, causing an increase in free thyroid hormone levels [18,41]. External cooling measures, such as alcohol sponging, ice packs, or a cooling blanket, can also be used. Fluid loss and dehydration are also common in severe thyrotoxicosis. The fluid losses could result from the combination of fever, diaphoresis, vomiting, and diarrhea. Intravenous fluids with dextrose (isotonic saline with 5% or 10% dextrose) should be given to replenish glycogen stores [41]. Patients should also receive multivitamins, particularly thiamine, to prevent Wernicke's encephalopathy, which could result from the administration of intravenous fluids with dextrose in the presence of thiamine deficiency [2].

Treating the precipitating cause of thyrotoxicosis is particularly important, considering that the most common precipitant is thought to be infection. If a precipitating factor were not readily apparent, a vigorous search for an infectious source would be warranted in the febrile thyrotoxic patient; this would be done with blood, urine, and sputum cultures, and a chest

radiograph or noncontrast CT. Generally, however, empiric antibiotics are not recommended without an identified source of infection. In cases of thyroid storm precipitated by diabetic ketoacidosis, myocardial infarction, pulmonary embolism, or other acute processes, appropriate management of the specific underlying problem should proceed along with the treatment of the thyrotoxicosis [4].

Perioperative management

The history of thyroid surgery, or surgery in the setting of thyrotoxicosis, began in the late nineteenth century with dismal results and high mortality. Much of the mortality associated with thyroid surgery in the past was because of postoperative thyroid storm. Even in the early twentieth century, mortality ranged from 8% with very experienced surgeons, to 20% in less experienced medical centers. In 1923, with the start of inorganic iodine use preoperatively, mortality rates decreased to less than 1% with experienced surgeons. Then, in the 1940s, thionamides began to be used in preoperative preparation of thyrotoxic patients. Finally, in the 1960s, preoperative beta-adrenergic receptor blockade with propranolol emerged, with even better outcomes [25].

Preoperative management of the thyrotoxic patient can be subdivided into two categories: preparation for elective or nonurgent procedures and preparation for emergent procedures. When rapid control of thyrotoxicosis is not required, as would be the case for an elective or nonurgent procedure, the standard course of therapy would be to achieve euthyroidism before surgery. In this situation, thionamide therapy would be recommended and would facilitate euthyroidism within several weeks [25]. The use of iodine as a method of decreasing thyroid vascularity and friability before thyroid surgery has been debated. Since the early twentieth century, when the routine use of iodine for preoperative preparation for thyroidectomy in the treatment of thyrotoxicosis began, surgeons have believed that iodine decreases thyroid gland vascularity and friability [25]. Several studies have shown some evidence that iodine treatment does decrease blood flow to the thyroid gland [64,65]. However, one retrospective study comparing surgical outcomes in 42 hyperthyroid patients who underwent subtotal thyroidectomy with propranolol treatment alone, or propranolol and iodine treatment, revealed no benefit in terms of blood loss intraoperatively [66]. Therefore, in the preparation of thyrotoxic patients for a nonemergent procedure, iodine use may be indicated only if thionamides cannot be tolerated.

In the preoperative preparation of thyrotoxic patients for emergent procedures, time is of the essence. Rapid lowering of thyroid hormone levels, control of thyroid hormone release, and control of peripheral manifestations of thyroid hormone are needed. In this situation, several regimens have been tried with success, using the same therapeutic modalities that are used in the treatment of thyroid storm [25]. Management of rapid preparation of

Table 4
Rapid preparation of thyrotoxic patients for emergent surgery

Drug class	Recommended drug	Dosage	Mechanism of action	Continue postoperatively?
Beta-adrenergic Blockade	Propranolol	40–80 mg po tid-qid	Beta-adrenergic blockade; decreased T4-to-T3 conversion (high dose)	Yes
	or			
	Esmolol	50–100 μg/kg/min	Beta-adrenergic blockade	Change to oral propranolol
Thionamide	Propylthiouracil	200 mg po q 4 h[a]	Inhibition of new thyroid hormone synthesis; decreased T4-to-T3 conversion	Stop immediately after near total thyroidectomy; continue after nonthyroidal surgery
	or			
	Methimazole	20 mg po q 4 h[a]	Inhibition of new thyroid hormone synthesis	Stop immediately after near total thyroidectomy; continue after nonthyroidal surgery
Oral cholecystographic agent	Iopanoic acid	500 mg po bid	Decreased release of thyroid hormone; decreased T4-to-T3 conversion	Stop immediately after surgery[b]
Corticosteroid	Hydrocortisone	100 mg po or IV q 8 h	Vasomotor stability; decreased T4-to-T3 conversion	Taper over first 72 h
	or			
	Dexamethasone	2 mg po or IV q 6 h	Vasomotor stability; decreased T4-to-T3 conversion	Taper over first 72 h
	or			
	Betamethasone	0.5 mg po q 6 h, IM or IV	Vasomotor stability; decreased T4-to-T3 conversion	Taper over first 72 h

[a] May be given per nasogastric tube or rectally.
[b] Not for prolonged use after nonthyroidal surgery in thionamide-intolerant patients.
From Langley RW, Burch HB. Perioperative management of the thyrotoxic patient. Endocrinol Metab Clin of North Am 2003;32:519–34; with permission.

thyrotoxic patients for emergent surgery is outlined in Table 4. One study used a 5-day course of betamethasone, iopanoic acid (no longer commercially available), and propranolol, with thyroidectomy performed on the sixth day in 14 hyperthyroid subjects. Rapid lowering of thyroid hormone levels occurred with good surgical outcomes [67].

Following thyroid surgery in hyperthyroid patients, therapy with beta-adrenergic receptor antagonists may still be required for a short period of

time because the half-life of T_4 is 7 to 8 days. However, after thyroidectomy, thionamide therapy usually can be stopped postoperatively, assuming that there is little thyroid tissue remaining. The authors tend to stop the antithyroid agents on days 1 to 3 postoperatively, depending on the clinical context. Preoperative management of hyperthyroidism aims to drive thyroid hormone levels to a euthyroid status before surgery. With adequately prepared hyperthyroid patients, morbidity and mortality due to thyroid or nonthyroid surgery is low [25].

Definitive therapy

Definitive therapy of thyrotoxicosis must be considered after the life-threatening aspects of thyroid storm are treated. As the thyrotoxic patient shows clinical improvement with therapy, some of the treatment modalities can be modulated or withdrawn; iodine therapy can be discontinued and glucocorticoids can be tapered. Thionamide therapy, at gradually decreasing doses, usually is required for weeks to months after thyroid storm, to attain euthyroidism. Beta-adrenergic receptor blockade is also needed while the patient is still thyrotoxic. Definitive therapy with radioactive iodine ablation may not be able to be used for several weeks or months following treatment with iodine for thyroid storm. Following the resolution of thyroid storm, the thyrotoxic patient continues to require close follow-up and monitoring, with plans for definitive therapy to prevent a future recurrence of life-threatening thyrotoxicosis [4].

Summary

Thyrotoxicosis and thyroid storm pose a critical diagnostic and therapeutic challenge to the clinician. Recognition of life-threatening thyrotoxicosis and prompt use of the arsenal of medications aimed at halting the thyrotoxic process at every level is essential to successful management. With the array of therapeutic interventions, treatment aimed at stopping synthesis of new hormone within the thyroid gland, halting the release of stored thyroid hormone from the thyroid gland, preventing conversion of T_4 to T_3, and providing systemic support of the patient can transition the thyroid storm patient out of critical illness. Once this transition occurs, definitive therapy of thyrotoxicosis can be planned.

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