Preparation for Anaesthesia - Thyroid Dysfunction

The major thyroid hormones are thyroxine (T_4), a product of the thyroid gland, and the more potent 3,5,3-triiodothyronine (T_3), a product of both the thyroid and the extrathyroidal enzymatic deiodination of thyroxine. Approximately 80 to 85 percent of T_3 is produced outside the thyroid gland. Production of thyroid secretions is maintained by secretion of thyroid-stimulating hormone (TSH) in the pituitary, which in turn is regulated by secretion of thyrotropinreleasing hormone (TRH) in the hypothalamus. Secretion of TSH and TRH appears to be negatively regulated by T_4 and T_3 . Whether all effects of thyroid hormones are mediated by T_3, or if T_4 has intrinsic biologic activity, remains unclear. Thyroid hormones create their effects through several mechanisms. Binding of T_3 to high-affinity nuclear receptors (TR_{alpha} and TR_{beta}) and the subsequent activation of DNA-directed mRNA synthesis may account for the anabolic growth and developmental effects, plus some calorigenic effect, of thyroid hormones. Patients with the syndrome of thyroid hormone resistance have point mutations in the TR_{beta} . Thyroid hormone is also responsible for an increased concentration of adrenergic receptors, which may account for many of its cardiovascular effects.
Because T_3 has a greater biologic effect than does T_4, one would expect the diagnosis of thyroid disorders to be based on levels of T_3 . However, this is not usually the case. The diagnosis of thyroid disease is confirmed by one of several biochemical measurements: levels of free T_4 or of total serum concentrations of T_4, and by the "free T_4 estimate." The estimate is obtained by multiplying total T_4 (free and bound) by the thyroid binding ratio (formerly called the resin T_3 uptake) (Table 25–12). The T_3 -binding ratio measures the extra quantity of serum protein binding sites. This measurement is necessary because thyroxine-binding globulin (TBG) is abnormally high during pregnancy, hepatic disease, and estrogen therapy (all of which would elevate the total T_4 level) (Table 25–13). Reliable interpretation of measurements of the total hormone concentration in serum necessitates data on the percentage of bound hormone. The thyroid hormone-binding ratio test provides this information. In this test, iodine-131-labeled T_3 is added to a patient's serum and allowed to reach an equilibrium binding state. A resin is then added that binds the remaining radioactive T_3 . The resin uptake is greater if the patient has fewer TBG binding sites. In normal patients, the resin T_3 uptake (the thyroid hormone-binding ratio) is 25 to 35 percent. When the serum TBG is elevated, the thyroid hormone-binding ratio is diminished (see Table 25–12). When the serum TBG is diminished, as in the nephrotic syndrome, in conditions in which glucocorticoids are increased, or in chronic liver disease, the thyroid hormone-binding ratio is increased.

TABLE 25–12. Biochemical Measurements of Thyroid Function That Account for Variation in Production of Thyroid-Binding Globulin

	EXAMPLES OF NORMAL THYROID STATUS					TSH
	FT_4E	=	T_4	×	THBR	
Normal	0.19 (0.12–0.25)	=	0.6 (0.4–0.9)		31% (25-35%)	0.2 (0.2–0.8)
During use of oral contraceptives	0.19	=	1.3		15%	0.3

TABLE 25–12. Biochemical Measurements of Thyroid Function That Account for Variation in Production of Thyroid-Binding Globulin						
	EXAMPLES OF NORMAL THYROID STATUS					TSH
	FT_4E	=	T_4	×	THBR	
During use of corticosteroids	0.18	=	0.3		60%	0.3
Abbreviations: FT_4E is the free T_4 (thyroxine) estimate. This is usually obtained by multiplying the total thyroxine (T_4) concentration (the free amount and the amount bound to protein) times the thyroid hormone binding ratio (THBR, formerly called the resin T_3 uptake). THBR is a measure of the bound thyroid hormone binding protein. TSH is the thyroid-stimulating hormone secreted by the pituitary in the negative feedback loop. (TSH increases when FT_4E is low in hypothyroidism.)						

TABLE 25–13. Factors Influencing Serum Levels of Thyroxine-Binding Globulin	
CONDITIONS INCREASING SERUM LEVELS	CONDITIONS DECREASING SERUM LEVELS
Use of oral contraceptives	Testosterone
Pregnancy	Use of corticosteroids
Use of estrogen	Severe illness
Infectious hepatitis	Cirrhosis
Chronic active hepatitis	Nephrotic syndrome
Neonatal state	Inherited conditions
Acute intermittent porphyria	?Phenytoin
Inherited conditions	

The free T_4 estimate and the free T_3 estimate are frequently used as measures of a patient's serum T_4 and T_3 hormone concentration. To obtain these estimates, the concentration of total serum T_4 or total serum T_3 is multiplied by the measured thyroid hormone-binding ratio. The values of these two indices are normal in the event of a primary alteration in binding, but not in secretion, of thyroid hormone.

Hyperthyroidism can be diagnosed by measuring the levels of TSH after administration of TRH. Although administering TRH normally increases TSH levels in blood, even a small increase in the T_4 or T_3 level in blood abolishes this response. Thus, a subnormal or absent serum TSH response to TRH is a very sensitive indicator of hyperthyroidism. [182] In one

group of disorders involving hyperthyroidism, serum TSH levels are elevated in the presence of elevated levels of free thyroid hormone.

Measurement of the a-subunit of TSH has been helpful in identifying the rare patients who have a pituitary neoplasm and who usually have increased a-subunit concentrations. Some patients are clinically euthyroid in the presence of elevated levels of total T_4 in serum. Certain drugs, notably gallbladder dyes, propranolol, glucocorticoids, and amiodarone, block the conversion to T_3 to T_4, thereby elevating T_4 levels. Severe illness also slows this conversion. Levels of TSH are often high in situations where the rate of this conversion is decreased. In hyperthyroidism, cardiac function and responses to stress are abnormal; return of normal cardiac function parallels the return of TSH levels to normal values.

Hyperthyroidism

Although hyperthyroidism is usually caused by the multinodular diffuse enlargement in Graves disease (also associated with disorders of the skin and/or eyes), it can also occur with pregnancy, [183] thyroiditis (with or without neck pain), thyroid adenoma, choriocarcinoma, or TSH-secreting pituitary adenoma. Five percent of women have thyrotoxic effects 3 to 6 months postpartum and tend to have recurrences with subsequent pregnancies. Major manifestations of hyperthyroidism are weight loss, diarrhea, warm moist skin, weakness of large muscle groups, menstrual abnormalities, nervousness, jitteriness, intolerance to heat, tachycardia, cardiac arrhythmias, mitral valve prolapse, [184] and heart failure. When the thyroid is functioning abnormally, the entity most threatened is the cardiovascular system. When diarrhea is severe, dehydration should be corrected preoperatively. Mild anemia, thrombocytopenia, increased serum alkaline phosphatase, hypercalcemia, muscle wasting, and bone loss frequently occur in hyperthyroidism. Muscle disease usually involves proximal muscle groups; it has not been reported to cause respiratory muscle paralysis. In the apathetic form of hyperthyroidism (seen most commonly in persons older than 60 years), cardiac effects dominate the clinical picture. [185] These signs and symptoms include weight loss, anorexia, and cardiac effects such as tachycardia, irregular heart rhythm, atrial fibrillation (in 10%), heart failure, and occasionally papillary muscle dysfunction. [184, 185]

Although b-adrenergic receptor blockade can control heart rate, its use is fraught with hazard in the patient already experiencing congestive heart failure (CHF). However, decreasing heart rate may improve heart pumping function. Thus, hyperthyroid patients who have fast ventricular rates, who are in CHF, and who require emergency surgery are given esmolol guided by changes in pulmonary artery wedge pressure and their condition. If slowing the heart rate with a small dose of esmolol (50 mg/kg) does not aggravate heart failure, the author administers more esmolol. I believe that we should aim to avoid imposing surgery on any patient whose thyroid function is clinically abnormal. Therefore, I believe only "life-or-death" emergency surgery should preclude making the patient pharmacologically euthyroid, a process that can take 2 to 6 weeks. Antithyroid medications include propylthiouracil or methimazole, both of which decrease the synthesis of thyroxine and may enhance remission by reducing TSH-receptor antibody levels (the primary pathologic mechanism in Graves disease). Propylthiouracil also decreases the conversion of T_4 into the more potent T_3 . However, the literature indicates a trend toward preoperative preparation with propranolol and iodides alone. [186] This approach is quicker (i.e., 7–14 d versus 2–6 wk); it shrinks the thyroid gland, as does the more traditional approach; and it treats symptoms but may not correct abnormalities in left ventricular function. [187] Regardless of approach, antithyroid drugs should be administered chronically and on the morning of surgery. If emergency surgery is necessary before the euthyroid state is achieved, if subclinical hyperthyroidism progresses without adequate treatment, [188] or if hyperthyroidism gets out of control during surgery, intravenous administration of esmolol,

50 to 500 mg/kg, should be titrated to restore normal heart rate (assuming the absence of congestive heart failure) (see previous). Also, intravascular fluid volume and electrolyte balance should be restored. However, administering propranolol or esmolol does not invariably prevent "thyroid storm." [189]

No controlled study has demonstrated clinical advantages of any anesthetic drug over another for surgical patients who are hyperthyroid. A review of cases performed at the University of California, San Francisco, from 1968 to 1982 reveals that virtually all anesthetic agents and techniques [190] have been employed without adverse effects being even remotely attributable to agent or technique. Furthermore, although some investigators have recommended that anticholinergic drugs (especially atropine) be avoided because they interfere with the sweating mechanism and cause tachycardia, atropine has been given as a test for adequacy of antithyroid treatment. Because patients are now subject to operative procedures only when euthyroid, the traditional "steal" of the heavily premedicated hyperthyroid patient (so commonly found in the iodine-deficient locales producing the Lahey, Mayo, and Cleveland Clinics) to the operating room has vanished.

The patient having a large goiter and an obstructed airway can be handled in the same way as any other patient having problematic airway management. Preoperative medication should avoid excessive sedation, and an airway should be established, often with the patient awake. A firm armored endotracheal tube is preferable and should be passed beyond the point of extrinsic compression. It is most useful to examine the CT scans of the neck preoperatively to determine the extent of compression. Maintenance of anesthesia usually presents little difficulty. Postoperatively, extubation should be performed under optimal circumstances for reintubation, in the event the tracheal rings have been weakened and the trachea collapses.

Of the many possible postoperative complications (nerve injuries, bleeding, and metabolic abnormalities), "thyroid storm" (discussed later), bilateral recurrent nerve trauma, and hypocalcemic tetany are the most feared. Bilateral recurrent laryngeal nerve injury (by trauma or edema) causes stridor and laryngeal obstruction due to unopposed adduction of the vocal cords and closure of the glottic aperture. Immediate endotracheal intubation is required, usually followed by tracheostomy to ensure an adequate airway. This rare complication occurred only once in more than 30,000 thyroid operations at the Lahey Clinic. Unilateral recurrent nerve injury often goes unnoticed because of compensatory overadduction of the uninvolved cord. However, we often test vocal cord function before and after this surgery by asking the patient to say "E" or "moon." Unilateral nerve injury is characterized by hoarseness, and bilateral nerve injury, by aphonia. Selective injury of adductor fibers of both recurrent laryngeal nerves leaves the abductor muscles relatively unopposed, and pulmonary aspiration is a risk. Selective injury of abductor fibers leaves the adductor muscles relatively unopposed, and airway obstruction can occur. Bullous glottic edema, an additional cause of postoperative respiratory compromise, has no specific cause or known preventive measure.

The intimate involvement of the parathyroid gland with the thyroid gland can result in inadvertent hypocalcemia during surgery for thyroid disease. Complications relating to hypocalcemia are discussed in the later section, *Hypocalcemia*.

Because postoperative hematoma can compromise the airway, neck dressings and wound dressings are placed in a crossing fashion (rather than vertically or horizontally) and should be examined for evidence of bleeding before a patient is discharged from the recovery room.

Thyroid Storm

Thyroid storm is the name for the clinical diagnosis of a life-threatening illness in a patient whose hyperthyroidism has been severely exacerbated by illness or operation. Thyroid

storm is manifested by hyperpyrexia, tachycardia, and striking alterations in consciousness. [191] Thyroid storm can thus present very similarly to malignant hyperthermia, pheochromocytoma, or the neuroleptic malignant syndrome. [150] No laboratory tests are diagnostic of thyroid storm, and the precipitating (nonthyroidal) cause is the major determinant of survival. Therapy can include blocking the synthesis of thyroid hormones by administering antithyroid drugs, blocking the release of preformed hormone with iodine, meticulous attention to hydration and supportive therapy, and correcting the precipitating cause. Blocking the sympathetic nervous system with reserpine, guanethidine, or a- and b-receptor antagonists may be exceedingly hazardous and requires skillful management and constant monitoring of the critically ill patient.

Hypothyroidism

Hypothyroidism is a common disease, occurring in 5 percent of a large population in Great Britain, in 3 to 6 percent of a healthy older population in Massachusetts, and in 4.5 percent of a medical clinic population in Switzerland. [192, 193] Usually hypothyroidism is subclinical, serum concentrations of thyroid hormones are in the normal range, and only serum TSH levels are elevated. The normal range of TSH being 0.3 to 4.5 mU/L, TSH values of 5 to 15 mU/L are characteristic of this entity. [193] In such cases, hypothyroidism may have little or no perioperative significance. However, a recent retrospective study of 59 mildly hypothyroid patients found that more hypothyroid patients than control subjects required prolonged postoperative intubation (9 of 59 versus 4 of 59) and had significant electrolyte imbalances (3 of 59 versus 1 of 59) and bleeding complications (4 of 59 versus 0 of 59). [194] Because only a small number of charts were examined, these differences did not reach statistical significance. In another study, a high percentage of patients with a history of subclinical hypothyroidism later developed overt hypothyroidism. [195] Thus, a prior history of subclinical hypothyroidism may indicate the need to search for, and be concerned about, the possibility of overt hypothyroidism.

In the less frequent occurrences of overt hypothyroidism, relative lack of thyroid hormone results in slow mental functioning, slow movement, dry skin, arthralgias, carpal tunnel syndrome, periorbital edema, intolerance to cold, depression of the ventilatory responses to hypoxia and hypercarbia, [196] impaired clearance of free water with or without hyponatremia, “hung-up reflexes,” slow gastric emptying, and bradycardia. In extreme cases, cardiomegaly, heart failure, and pericardial pleural effusions manifest as fatigue, dyspnea, and orthopnea. [197] Hypothyroidism is often associated with amyloidosis, which may produce an enlarged tongue, abnormalities of the cardiac conduction system, and renal disease. Hypothyroidism decreases anesthetic requirement slightly. [198] The tongue may be enlarged in the hypothyroid patient even in the absence of amyloidosis, and this may hamper endotracheal intubation.

A rising TSH level is a most sensitive indicator of failing thyroid function. Ideal preoperative management of hypothyroidism consists of restoring normal thyroid status: I routinely administer the normal dose of T_3 or T_4 the morning of surgery, even though these drugs have long half-lives (1.4–10 d). Reduced gastrointestinal absorption of levothyroxine may occur with coadministration of cholestyramine or aluminum hydroxide, iron, a high-bran meal, or sucralfate or colestipol. For patients with myxedema coma requiring emergency surgery, T_3 can be given intravenously (with fear of precipitating myocardial ischemia, however) while supportive therapy is undertaken to restore normal intravascular fluid volume, body temperature, cardiac function, respiratory function, and electrolyte balance. Treating hypothyroid patients having symptomatic coronary artery disease poses special problems and may require compromises in the general practice of preoperatively restoring euthyroidism with drugs. [197] Although both T_4 and esmolol may be given, adequate amelioration of both ischemic heart disease and hypothyroidism may be difficult to achieve.

The need for thyroid therapy must be balanced against the risk of aggravating anginal symptoms. One review suggested early consideration for coronary artery revascularization.[199] It advocated initiating thyroid replacement therapy in the ICU soon after the patient's arrival from the operating room and myocardial revascularization surgery. However, several deaths due to arrhythmia and CHF as well as cardiogenic shock with infarction have occurred while patients who were not given thyroid therapy were awaiting surgery. Thus, there is need for consideration of true emergency coronary artery revascularization in patients having both severe coronary artery disease and significant hypothyroidism.

In hypothyroidism, respiratory control mechanisms do not function normally.[196] However, the response to hypoxia and hypercarbia and the clearance of free water become normal with thyroid replacement therapy.[196, 197] Drug metabolism is anecdotally reported to be slowed, and awakening times from sedatives are reported to be prolonged during hypothyroidism. However, no formal study of the pharmacokinetics and pharmacodynamics of sedatives or anesthetic agents has been published. These concerns disappear when thyroid function is normalized preoperatively. Addison disease (with its relative steroid deficiency) is more common in hypothyroidism, and some endocrinologists routinely treat noniatrogenic hypothyroid patients with stress doses of steroids perioperatively, as both conditions are commonly caused by autoimmune responses. The possibility that this steroid deficiency exists should be considered if the patient becomes hypotensive perioperatively. Body heat mechanisms are inadequate in hypothyroid patients, and temperature should be monitored and maintained, especially in patients requiring emergency surgery. Because there is an increased incidence of myasthenia gravis in hypothyroid patients, it may be advisable to use a peripheral nerve stimulator to guide administration of muscle relaxants (Ch. 36).

Thyroid Nodules and Carcinoma

Identifying malignancy in a solitary thyroid nodule is a difficult and important procedure. Male patients and patients with previous radiation to the head and neck have an increased likelihood of malignant disease in their nodules. Often, needle biopsy and scanning are sufficient for the diagnosis, but occasionally an excisional biopsy is needed. Papillary carcinoma accounts for more than 70 percent of all thyroid carcinomas. Simple excision of lymph node metastases appears to be as efficacious for patient survival as are radical neck procedures. Follicular carcinoma accounts for about 15 percent of thyroid carcinomas, is more aggressive, and has a less favorable prognosis.

Medullary carcinoma is the most aggressive form of thyroid carcinoma. It is associated with a familial incidence of pheochromocytoma, as are parathyroid adenomas. For this reason, a history might be obtained for patients who have a surgical scar in the thyroid region, so that the possibility of occult pheochromocytoma can be ruled out.