

# Patients with Chronic Endocrine Disease

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## KEYWORDS

- Diabetes mellitus • Adrenal insufficiency • Hyperthyroidism • Hypothyroidism
- Acromegaly • Pheochromocytoma • Carcinoid

## KEY POINTS

- The goal of preoperative management of chronic endocrine disease is to minimize the impact of the associated comorbidities on the perioperative course by maintaining physiologic and metabolic homeostasis.
- There are few evidence-based guidelines for preoperative management of chronic endocrine disease; hence this review is based on recent subspecialty society consensus guidelines and professional society clinical practice recommendations.
- This review summarizes the key features and clinical considerations related to preoperative management and planning for the care of patients of common endocrine disorders (diabetes mellitus, adrenal insufficiency, thyroid disease), a less common disorder but one that has significant perioperative implications (acromegaly), and 2 disorders for which preoperative management is essential to good postoperative outcomes (pheochromocytoma and carcinoid syndrome).

## INTRODUCTION

The American Society of Anesthesiologists Committee on Standards and Practice Parameters recently published the updated practice advisory for the preparation of patients for surgery.<sup>1</sup> Although the standards are designed to assist in basic decision making by the anesthesiologist, one aspect of these guidelines should be highlighted: the importance of the integration of pertinent information for the appropriate assessment of the severity of the patient's medical condition in advance of the procedure. In addition to perioperative management, the practitioner who cares for the patient with endocrine disease is important in the coordination of patient care, including providing information related to risk stratification, assessment of the extent of disease control, defining the current state of hormonal-metabolic balance, and providing guidance

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for perioperative pharmacologic and medical management. For perioperative testing, the cost of repeating endocrine assays for the sole purpose of preprocedure documentation may be prohibitive. Selective tests may be repeated when the information may assist in optimizing perioperative care or if the course of care will be altered by the additional information.

There are few randomized controlled trials and evidence-based guidelines related to preoperative management of patients with endocrine disease. The majority of recommendations are adapted from meta-analyses, professional society consensus statements, and current literature reviews. Some endocrinopathies may not result in chronic disease because the medical and/or surgical therapy to control or eradicate the disease (eg, pheochromocytoma) is sufficient. Other endocrinopathies (eg, diabetes, acromegaly, recurrent carcinoid) may result in chronic disease because of the range of comorbidities that occur with or without treatment.

## DIABETES MELLITUS

Since 2001, the literature related to glycemic control has been extensive, probably influenced by the increasing number of diagnosed and undiagnosed diabetics presenting for medical care, and the recognition of the relationship between blood glucose variability and adverse outcomes.<sup>2-4</sup> The proponents of tight glycemic control (blood glucose target 80–110 mg/dL) recognized the relationship between the severity of hyperglycemia and the extent of a myocardial infarction<sup>5</sup>; the association between fasting glucose and the risk of cardiovascular events in patients with and without diabetes<sup>6</sup>; reduced morbidity and mortality among critically ill patients with a stay in the intensive care unit (ICU) of longer than 3 days; and reduced morbidity, including the prevention of newly acquired kidney injury, accelerated weaning from mechanical ventilation, and decreased length of stay in the ICU and hospital.<sup>3</sup> As a result, tight glycemic control and intensive insulin therapy were incorporated into the standards of care in many centers, and glycemic control has been used as a hospital performance measure by the National Hospital Inpatient Quality Measure (NHIQM), the Surgical Care Improvement Project (SCIP), and the Joint Commission (JC), and is a component of Pay for Performance (P4P). Since 2009 intensive glucose control has been reevaluated, recognizing that tight glycemic control targets increase the risk of severe hypoglycemia (blood glucose 40 mg/dL) in some patients, may increase mortality risk, and may only benefit specific patient populations (eg, the critically ill and brittle diabetics).<sup>7,8</sup>

In 2009, the American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) updated the Consensus Statement on inpatient glycemic management, providing less stringent glycemic targets for critically ill and non-critically ill patients, and recommendations for treatment options and monitoring.<sup>9</sup> The recommendations (**Box 1**) include the administration of insulin to critically ill patients for persistent serum glucose level of 180 mg/dL and higher to achieve a target of 140 to 180 mg/dL. The glucose target for non-critically ill patients receiving insulin is less than 140 mg/dL when fasting and less than 180 mg/dL for random measurements. Scheduled, subcutaneous insulin with basal nutritional and correction components are recommended for achieving and maintaining control in the noncritical population. In addition, noninsulin agents are not suitable for most hospitalized patients who require treatment of hyperglycemia because of their pharmacokinetics and variable half-lives, making the agents less amenable to rapid titration.

Because the AACE-ADA recommendations did not specifically address patients undergoing ambulatory surgical procedures, the Society for Ambulatory Anesthesia

**Box 1****Summary of AACE-ADA consensus on inpatient glycemic control***Critically Ill Patients: Treat with Intravenous Insulin*

- Initiate insulin infusion, for persistent hyperglycemia 180 mg/dL or greater
- Use validated protocols
- Glucose target 140 to 180 mg/dL

*Non-Critically Ill Patients*

- If treated with subcutaneous insulin
  - Premeal blood glucose less than 140 mg/dL
  - Random blood glucose less than 180 mg/dL
  - Scheduled subcutaneous insulin with basal, nutritional, correction components
- Reassess insulin regimen if blood glucose levels less than 100 mg/dL

*Noninsulin Agents*

- Not recommended for hyperglycemia treatment of hospitalized patients
- May be appropriate in selected patients

*Data from* Moghissi E, Korytkowski M, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Endocr Pract* 2009;15(4):1–17.

(SAMBA) developed a consensus statement on blood glucose management in diabetic patients.<sup>10</sup> The recommendations, a result of a systematic review of the literature from January 1980 to November 2009, are based on general principles of blood glucose control in diabetics, drug pharmacology, data gathered from inpatient surgical populations, review articles, clinical experience, and judgment. These guidelines are summarized in **Box 2**. The SAMBA recommendations for preoperative management include an assessment of the level of glycemic control with measurement of glycosylated hemoglobin, documentation of the types and doses of antidiabetic agents, assessment of the frequency and symptoms of hypoglycemia, and an assessment of the patient's level of understanding and participation in self-management.

For patients who are treated with oral hypoglycemic and noninsulin injectable agents, the SAMBA recommendation is to withhold the medicine on the day of surgery until normal oral intake resumes. For patients treated with insulin, the recommendation is to continue basal insulin unless there is a history of hypoglycemia. For the patient who is fasting before surgery, insulin regimens are summarized as follows: (1) no change required for continuous subcutaneous insulin pump but may reduce to sleep basal rates; (2) decrease morning dose of intermediate-acting and fixed combination insulin doses by 50% to 75%; (3) hold short-acting and rapid-acting insulin on the morning of surgery. The goals of perioperative ambulatory management are to minimize fluctuations in the glycemic management regimen, avoid hypoglycemia, and resume oral intake, when appropriate, soon after surgery.

In 2013, the ADA revised the standards of medical care in diabetes, based on new evidence published since 2011. The ADA guidelines are intended for use in conjunction with clinical judgment by patients and clinicians who manage diabetes.<sup>11</sup> Although the guidelines do not specifically address preoperative management of the patient with diabetes, the recommendations related to chronic management are relevant. The content related to the assessment of glycemic control, pharmacologic

**Box 2****SAMBA consensus statement on blood glucose management in diabetic patients for ambulatory surgery***Preoperative Information Related to Glycemic Control*

- Hemoglobin A<sub>1c</sub>
- Type and dose of antidiabetic therapy
- Hypoglycemia: occurrence, frequency, manifestations, blood glucose at which symptoms occur
- Hospitalizations related to glycemic control
- Assess patient's ability to reliably test glucose and manage diabetes

*Management of Preoperative Oral Antidiabetic and Noninsulin Injectible Therapy*

- Hold on the day of surgery until normal food intake is resumed

*Management of Preoperative Insulin Therapy*

- Day before surgery
  - No change in basal insulin regimen, unless history of hypoglycemia
- Day of surgery
  - Insulin pump: no change
  - Long-acting insulin: 75% to 100% of morning dose
  - Intermediate-acting insulin and fixed-combination insulin: 50% to 75% of morning dose
  - Short-acting, rapid-acting, and noninsulin injectables: hold morning dose

*Optimal Intraoperative Blood Glucose Level*

- Well-controlled diabetes: less than 180 mg/dL
- Poorly controlled diabetes: maintain preoperative baseline values
  - Hypoglycemic symptoms may occur at normal blood glucose levels

*Regimen to Maintain Optimal Blood Glucose Level*

- Subcutaneous rapid-acting insulin analogues
- Dosing schedule based on time to peak effect

*Optimal Perioperative Blood Glucose Monitoring*

- Measure blood glucose level before surgery and before discharge home
- Intraoperative blood glucose monitoring every 1 to 2 hours, depending on duration and type of insulin

*Hypoglycemia Management*

- Diagnosis
  - Glucose less than 70 mg/dL or
  - Based on symptoms: sweating, palpitations, weakness, fatigue, confusion, behavioral changes, seizure, altered level of consciousness
- Treatment
  - Glucose 10 to 25 g, oral or intravenous
  - Glucagon 1 mg subcutaneously, if unable to ingest or if no intravenous access

*Other Considerations:*

- Preoperative hydration
- Nausea and vomiting prophylaxis

*Data from* Joshi GP, Chung F, Vann MA, et al. SAMBA consensus statement on perioperative blood glucose management in diabetic patients undergoing ambulatory surgery. *Anesthesiology* 2010;111(6):1378–87.

treatment, intercurrent illness and hypoglycemia, and discharge planning are applicable to the care of the patient preparing for surgery (**Box 3**).

Based on the 2012 American College of Physicians Clinical Practice Guidelines, there are more than 11 unique classes of oral pharmacologic agents used for the treatment of type 2 diabetes (**Box 4**). Metformin is first-line monotherapy, when not contraindicated. When monotherapy is inadequate because of failure to reach glycemic targets, the addition of a second agent (combination therapy) is recommended, and at times insulin therapy may be required. Hypoglycemia is more common with sulfonamides and with metformin-sulfonurea combination therapy. The thiazolidinediones are associated with an increased risk of heart failure, and may be contraindicated in patients with preexisting serious heart failure.<sup>12</sup> Metformin has been associated with lactic acidosis, but it is not clear if the lactic acidosis is due to the accumulation of metformin in patients with renal dysfunction (creatinine >1.4) or if this occurs in patients who are predisposed to lactic acidosis or renal insufficiency, independent of metformin therapy (eg, hypoxemia, shock, acute myocardial infarction, acute congestive heart failure, liver dysfunction, surgery, intravenous contrast administration). Because

### Box 3

#### American Diabetes Association standards of medical care in diabetes

##### *Glycemic Recommendations for Nonpregnant Adults with Diabetes*

- Hemoglobin A<sub>1c</sub> less than 7%
- Peak preprandial (before meals and snacks) capillary plasma glucose 70 to 130 mg/dL
- Peak postprandial capillary plasma glucose less than 180 mg/dL

##### *Individual Goals Based On:*

- Duration of diabetes
- Age/life expectancy
- Comorbid conditions
- Cardiovascular or microvascular complications
- Hypoglycemia unawareness

##### *Pharmacologic Management*

###### Type 1 diabetes

- Three to 4 injections of basal and postprandial insulin or subcutaneous insulin infusion

###### Type 2 diabetes

- Metformin, preferred initial agent
- Add second oral agent or insulin, if first-line therapy at maximal tolerated dose or hemoglobin A<sub>1c</sub> greater than target

##### *Hypoglycemia (Glucose < 70 mg/dL)*

- Assess for symptomatic and asymptomatic hypoglycemia
- Treatment
  - Glucose 15 to 20 g (intravenous or oral)
  - Glucagon 0.5 to 1 IU (subcutaneous, intravenous, intramuscular)
  - Reassess glycemic targets

*Data from* American Diabetes Association. Standards of medical care in diabetes—2013. Diabetes Care 2013;36(Suppl 1):S11–66.

<b>Box 4</b>		
<b>Pharmacologic treatment options for diabetes</b>		
<b>Oral Antidiabetic Agents</b>	<b>Noninsulin Injectables</b>	<b>Insulin</b>
Metformin	Exenatide	Short to rapid acting:
Chlorpropamide	Pramlintide	Regular
Tolbutamide		Lispro
Glimepiride		Aspart
Glipizide		Glulisine
Glyburide		Intermediate acting:
Repaglinide		NPH insulin
Nateglinide		Zinc insulin
Rosiglitazone		Long acting:
Pioglitazone		Glargine
Acarbose		Detemir
Miglitol		Mixed insulins
Sitagliptin		
Saxagliptin		

*Data from Joshi GP, Chung F, Vann MA, et al. SAMBA consensus statement on perioperative blood glucose management in diabetic patients undergoing ambulatory surgery. Anesthesiology 2010;111(6):1378–87.*

of the benefits (lower all-cause mortality, decreased cardiovascular mortality, fewer hypoglycemic episodes) in the management of type 2 diabetes in conjunction with lifestyle modification, metformin continues to be first-line therapy; and unless there is a contraindication to its use, metformin should be continued in the perioperative period.<sup>12</sup>

Hyperglycemic crises, diabetic ketoacidosis (DKA), and hyperosmolar hyperglycemic state (HHS) are associated with high mortality. Surgery for patients who present with a hyperglycemic crisis should be postponed for treatment and for the identification and management of the precipitating cause. The diagnostic criteria for DKA and HHS, as summarized by Kitabchi and colleagues,<sup>13</sup> are outlined in **Table 1**. For the

	<b>DKA</b>			<b>HHS</b>
	<b>Mild</b>	<b>Moderate</b>	<b>Severe</b>	
Plasma glucose (mg/dL)	>250	>250	>250	>600
Arterial pH	7.25–7.3	7.00 to <7.24	<7.00	>7.30
Serum HCO <sub>3</sub> <sup>-</sup> (mEq/L)	15–18	10 to <15	<10	>18
Urine or serum ketone	+	+	+	Small
Effective serum osmolality	Variable	Variable	Variable	>320 mOsm/kg
Anion gap	>10	>12	>12	Variable
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

*Data from Moghissi E, Korytkowski M, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. Endocr Pract 2009;15(4):1–17.*

patient who presents on the day of surgery with hyperglycemia (glucose  $\geq 250$  mg/dL), the suggested approach is to determine whether there has been an intercurrent illness, a change in medication management, or another precipitating cause. The initial laboratory assessment should include plasma glucose, serum electrolytes, bicarbonate, blood urea nitrogen (BUN), creatinine, serum osmolality, serum or urine ketones, and the calculation of anion gap. If there is no identified precipitating cause, if the serum bicarbonate, osmolality, and anion gap are normal, and ketones are not present, then it is reasonable to proceed with the procedure, provided that the glucose decreases with hydration and insulin. If the response to treatment is considered inadequate or if in the clinician's judgment the risk outweighs the benefit, elective surgery should be postponed until the hyperglycemia, DKA, or HHS are resolved, until the patient has returned to the regimen that preceded the hyperglycemia, or until the glyce-mic treatment regimen is less variable and the glucose is stable.

Continuous glucose monitoring (CGM), together with intensive insulin therapy with subcutaneous insulin infusion delivered by pump, is being used increasingly for patients with type 1 diabetes. CGM devices can be continued during surgery as long as the device does not interfere with the surgical field.<sup>14</sup> The CGM glucose value should be confirmed with a serum measurement. When the patient is not receiving oral intake, the insulin delivery device should be reset to the patient's usual fasting dose.

## ADRENAL INSUFFICIENCY

Adrenal insufficiency (AI) is classified based on the site of hypothalamic-pituitary-adrenal (HPA) axis dysfunction. Primary AI is the result of failure of the adrenal gland. The most common causes of primary AI are autoimmune adrenalitis, infection, post-surgical adrenalectomy, and sepsis. Secondary AI is the result of inadequate corticotropin for stimulation of the adrenal cortex, which may be due to atrophy of the adrenal cortex or exogenous glucocorticoid suppression of pituitary corticotropin. Common conditions associated with secondary AI include the therapeutic use of steroids to treat autoimmune disease, inflammatory disease, chronic lung disease, or asthma, or when steroids are used for organ transplantation. Tertiary AI is caused by impaired ability of the hypothalamus to secrete corticotropin-releasing hormone (CRH). In patients receiving a chronic replacement dose of steroids, the incidence of perioperative AI is probably low, and most reports of suspected AI are not based on biochemical confirmation. In practice, many patients receive perioperative steroid replacement, often in supraphysiologic doses. This practice is probably based on a 1994 recommendation for steroid replacement related to the degree of surgical stress.<sup>15,16</sup> In 2008, Marik and Varon<sup>17</sup> reviewed the literature from the period 1966 to 2007 related to perioperative stress-dose steroids for patients' undergoing surgical procedures. Their findings and recommendations recognize the differences in stress responses for patients receiving therapeutic doses of corticosteroids (eg, immunosuppression regimen after transplantation), but with an intact, though suppressed, HPA axis and stress response in patients with primary dysfunction of the HPA axis (eg, primary or secondary adrenal failure, Addison disease, congenital adrenal hyperplasia, hypopituitarism) requiring physiologic replacement. The recommendations based on their review are summarized in **Box 5**. The recommended doses of hydrocortisone are based on the physiologic responses to the stress of the surgical procedure as described by Salem and colleagues.<sup>16</sup>

For the practitioner managing the patient with chronic AI, the preoperative management and preparation should include the medical history, including the etiology of AI,

**Box 5****Perioperative stress doses of corticosteroids***Patients Receiving Therapeutic Doses of Corticosteroids (eg, organ transplant)*

- Continue usual daily dose
- No stress dose required
- No need to test adrenal function
- Consider stress dose in patients with volume refractory hypotension
  - Hydrocortisone 100 mg intravenously then 50 mg every 6 hours, until symptom resolution

*Patients Receiving Physiologic Replacement Doses of Corticosteroids (eg, primary AI)*

- Hydrocortisone 50 mg intravenously (one dose), for minor surgery
- Hydrocortisone 50 mg intravenously every 8 hours, for 48 to 72 hours, for major surgery

the history of previous adrenal crises and the precipitating cause(s), the chronic medication replacement regimen including dose and frequency, and the history of any medical or physiologic changes that may predispose to acute adrenal dysfunction. Laboratory evaluation should include electrolytes, BUN, creatinine, and glucose. The decision to administer steroids should be based on: the normal diurnal cortisol secretion in the absence of HPA dysfunction; chronic steroid dose; duration of treatment; anticipated recovery from HPA suppression after cessation of treatment; and the route of chronic steroid administration (topical, inhaled, oral, or intravenous).

Replacement is usually required for patients taking steroid doses that exceed a daily dose of 5 mg prednisone, 25 mg hydrocortisone, 4 mg triamcinolone, or 0.75 mg dexamethasone. The recommended replacement is a single dose of 50 mg hydrocortisone for minor surgery, and for major surgery 50 mg, 3 times a day, for 48 to 72 hours. For those patients receiving therapeutic doses of corticosteroids, the recommendation is to continue the usual daily dose prior to and including the day of surgery. Additional stress-dose steroids are usually not required.

The utility of repeating preoperative adrenal function tests is limited. If a patient develops hypotension during a procedure that is refractory to administration of intravenous fluids, the recommendation is to administer an initial dose of 100 mg hydrocortisone, followed by 200 mg/d (eg, 50 mg every 6 hours). Hydrocortisone is then continued until the stress resolves and when the patient is able to resume the preoperative steroid regimen. Mineralocorticoid replacement (fludrocortisone or equivalent) is usually not required unless it is a component of the chronic replacement regimen for primary AI. Moreover, hydrocortisone has mineralocorticoid activity in doses that exceed 100 mg/d and in the absence of primary adrenal failure. Most patients with AI do not show signs of aldosterone deficiency because mineralocorticoid secretion is primarily modulated by the renin-angiotensin system.

**THYROID DISEASE**

The goal of perioperative management of the patient with thyroid disease is to maintain the euthyroid state. In 2012, the AACE together with the American Thyroid Association published clinical practice guidelines for the management of hypothyroidism in adults.<sup>18</sup> Similarly, in 2011, evidence-, expert-, and consensus-based guidelines were developed for the management of hyperthyroidism.<sup>19</sup> Both these sets of recommendations refer to the management of the ambulatory patient with previously established hypothyroidism or hyperthyroidism.

The symptoms of hypothyroidism can be subclinical or overt. Dry skin, cold sensitivity, fatigue, muscle cramps, voice changes, and constipation are common symptoms. Hypothyroidism may be associated with a prolonged ankle-jerk relaxation time, carpal tunnel syndrome, bradycardia, and sleep apnea. A low serum thyrotropin level is the primary marker of the disease. L-Thyroxine is the primary treatment. Therapeutic end points for the management of hypothyroidism are related to resolution of symptoms, return to a normal resting heart rate, and normalization of cholesterol, anxiety, sleep pattern, menstrual cycle, creatinine kinase, hepatic transaminases, and thyrotropin levels.

Hyperthyroidism, a subset of thyrotoxicosis, is due to increased synthesis and secretion of thyroid hormone by the thyroid gland. Thyroid hormone excess increases basal metabolic rate and thermogenesis, reduces systemic vascular resistance, and may result in weight loss, tachycardia, atrial fibrillation, heart failure, neuropsychiatric dysfunction, anxiety, emotional lability, irritability, and muscle weakness and tremor. The primary treatment is  $\beta$ -blockade (propranolol, atenolol, metoprolol, nadolol, esmolol) for control of a heart rate in excess of 90 beats/min or for patients with concomitant cardiovascular disease. Oral calcium-channel blockers (verapamil, diltiazem) may be effective alternative agents for control of heart rate in patients with  $\beta$ -blocker intolerance.

The management of the patient with chronic thyroid dysfunction requires an assessment of symptoms, documentation of the medication regimen, and a detailed assessment of cardiovascular symptoms to elicit the presence of arrhythmias, heart failure, or ischemic heart disease. The primary purpose of the preoperative and preprocedure management is to establish and maintain the euthyroid state. For patients with a history of hypothyroidism, oral thyroid hormone replacement therapy should continue through the day of surgery and afterward. For patients with a history of hyperthyroidism,  $\beta$ -adrenergic blockade and the usual doses of antithyroid medications (propylthiouracil, methimazole, potassium iodide) should continue perioperatively. Propylthiouracil is associated with agranulocytosis, and methimazole and propylthiouracil are associated with hepatotoxicity. In some patients, hyperthyroidism may be associated with elevated liver enzymes. Patients receiving antithyroid agents may require baseline preoperative laboratory screening, including white blood cell count and differential and liver enzymes.

Changes in thyroid size, position, shape, and nodularity may influence the management of the airway. The physician responsible for the chronic care of the patient may be the first to elicit the symptoms associated with airway compromise and the potentially challenging perioperative airway. Findings that may be associated with airway changes are neck discomfort, stridor, swelling, dysphagia, hoarseness, changes in voice, and positional symptoms. The physical examination should include the position of the trachea and an assessment for positional dyspnea or dysphagia. Preprocedure imaging (chest radiograph, computed tomography scan) can help in evaluating the degree of tracheal compression or displacement. In some cases, flexible fiberoptic examination of the larynx may be needed to document the ease of access to the glottis as well as the preprocedure or preintubation position and function of the vocal cords.

Thyroid storm, or life-threatening thyrotoxicosis, may occur preoperatively, and is related to the abrupt cessation of antithyroid drugs, unrecognized or inadequately treated thyrotoxicosis, or exposure to exogenous iodine. The diagnosis requires a high index of suspicion in the presence of symptoms of thermoregulatory dysfunction, hemodynamic lability, gastrointestinal symptoms, and central nervous system disturbance.<sup>19</sup> The treatment of thyroid storm targets each step in thyroid hormone synthesis,

release, and site of action. Conversion of triiodothyronine to thyroxine is blocked by  $\beta$ -adrenergic blockade, Propylthiouracil, and corticosteroids. Synthesis of new thyroid hormone is blocked by methimazole and inorganic iodide. Moreover, inorganic iodide blocks the release of thyroid hormone. Symptomatic treatment also includes acetaminophen, cooling, and volume replacement. If the symptoms of thyrotoxicosis are recognized in advance, surgery should be postponed until the patient is rendered euthyroid. Consultation with an endocrinologist is indicated for the management of thyrotoxicosis, and for the management of hyperthyroidism in children, pregnant women, patients with concomitant cardiac disease, or if present with another complicated endocrine disease (AI) or when there is difficulty achieving a euthyroid state.

## ACROMEGALY

Excess of growth hormone (GH) is associated with multisystem comorbidities, and the presenting features depend on the timing of GH hypersecretion. If GH excess occurs before the closure of the epiphyseal plates, the result is accelerated vertical growth and, sometimes, gigantism. If GH excess occurs after epiphyseal closure, the result is acromegaly. Acromegaly is characterized, on physical examination, by enlargement of the skull, hands, and face; large tongue; protrusion of the brow and jaw; swelling of vocal cords; and a deep voice. In 2009, the Acromegaly Consensus Group published consensus guidelines for disease management.<sup>20</sup> In 2011, the AACE published updated guidelines for the diagnosis and treatment of acromegaly.<sup>21</sup> Although the guidelines do not specifically address the patient with GH excess who is presenting for nonpituitary surgery or other procedures, they do provide a comprehensive framework for assessing and managing the patient. The 2011 recommendations of the AACE are summarized in **Box 6**.

Acromegaly is associated with several comorbidities that may affect or confound perioperative management, including somatic enlargement, jaw overgrowth, joint pain, and carpal tunnel syndrome. Osteoarthropathy may affect the access to the operative site and positioning of the patient for surgery. Jaw overgrowth may influence the ability to achieve adequate mask fit and maintain airway patency, and may adversely affect the ability to achieve bag-mask ventilation. Central sleep apnea, which results in altered respiratory control, and obstructive sleep apnea as a result of craniofacial and soft-tissue changes, are associated with acromegaly. Patients with acromegaly and sleep apnea warrant more intense postprocedural monitoring and vigilance because of the increased sensitivity of the central nervous system (CNS) to the respiratory depressant effects of narcotics and sedatives, the associated risk of airway obstruction (macroglossia, epiglottis hypertrophy), and an attenuated hypoxic respiratory drive. GH-associated CNS changes (headaches, visual changes), may confound the postoperative assessment of a neurologic change. Complete documentation of the patient's baseline may save the cost of repeating tests and may facilitate timely assessment of new findings in the perioperative period.

Therapeutic options for acromegaly are medical, surgical, and radiation. Medical therapy is based on 3 types of agents: dopamine antagonists, somatostatin analogues, and GH receptor antagonists. The dopamine antagonists cabergoline and bromocriptine may cause nausea, vomiting, orthostatic hypotension, headache, and nasal congestion. Cabergoline has been associated with echocardiographic valvular abnormalities in patients who also have Parkinson's disease. The somatostatin analogues octreotide and lanreotide may cause nausea, poor glycemic control, and bradycardia. The GH receptor antagonist pegvisomant may cause enlargement of pituitary tumor, flu-like symptoms, allergic reactions, and increased liver enzymes.

**Box 6****Acromegaly: comorbidities influencing perioperative management**

<b>Acral</b>	<b>Cardiovascular</b>	<b>Pulmonary</b>	<b>Endocrine</b>	<b>Neurologic</b>	<b>Other</b>
Somatic enlargement	Cardiomyopathy, left ventricular hypertrophy, impaired systolic and diastolic function,	Sleep apnea	Diabetes mellitus	Headache	Fatigue
Jaw overgrowth	arrhythmias, conduction abnormalities		Menstrual irregularities	Visual field loss	Generalized weakness
Arthralgias	Hypertension		Hyper- and Hypoprolactinemia	Diplopia	Diaphoresis
Osteoarthropathy			Primary hyperparathyroidism associated with multiple endocrine neoplasia (MEN)-1		
			Post-therapy hypopituitarism		

*Data from* Katznelson L, Atkinson JL, Cook DM, et al, American Association of Clinical Endocrinologists. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of acromegaly—2011 update. *Endocr Pract* 2011;17(Suppl 4):1–44.

For the preparation of the patient with GH excess for nonpituitary surgery, the following points should be considered:

- Perform a comprehensive history, documentation of physical findings, and medication regimen including side effects.
- Obtain laboratory evaluation including electrolytes, glucose, BUN, creatinine, and liver function tests when indicated. Once the diagnosis of GH excess is established, repeat assays for GH, insulin-like growth factor I, oral glucose tolerance test, or prolactin are usually not needed preoperatively.
- Assess cardiovascular risk with testing based on risk profile, and signs and symptoms.
- Anticipate additional perioperative monitoring and the use of continuous positive airway pressure (if used preoperatively) if the patient has sleep apnea.
- If pituitary surgery has been performed previously, consider additional screening for symptoms of pituitary failure, hypothyroidism, adrenal dysfunction, syndrome of inappropriate antidiuretic hormone secretion, and diabetes insipidus; and plan for hormone supplementation when indicated.

## NEUROENDOCRINE TUMORS

Functional and nonfunctional neuroendocrine tumors originate from several tissue sites. The diseases may occur sporadically or as part of a familial genetic syndrome. Because the diseases are numerous, this review focuses on the preoperative preparation of patients with pheochromocytoma and carcinoid syndrome.

Pheochromocytomas are neuroendocrine tumors that present with symptoms of adrenergic excess as result of the production, storage, and secretion of catecholamines and their metabolites. The most common presenting signs are hypertension, palpitations, headache, diaphoresis, and pallor. Less common findings are fatigue, nausea, weight loss, constipation, flushing, and fever. The signs and symptoms are similar to other disease presentations and are not specific to pheochromocytoma, so the initial diagnosis may be missed in the absence of biochemical confirmation. Morbidity is due to the effects of catechol excess on end organs, including the cardiovascular system. The North American Neuroendocrine Tumor Society Consensus Guidelines were developed in 2010 to provide a standardized framework for the diagnosis, management of symptoms, selection of medical therapy, indications for surgery for focal disease, and options for management of advanced disease, which may include radiotherapy and systemic chemotherapy.<sup>22,23</sup> Although the primary goal of surgery is curative, some patients develop advanced, multifocal disease that is not amenable to surgical resection.

The goals for preoperative management for endocrine and nonendocrine surgery for the patient with pheochromocytoma are similar (**Box 7**). The preprocedure preparation includes an assessment of the current symptoms and signs of the disease, the current medical therapy, medication doses and frequency, and screening for and management of concomitant end-organ dysfunction (cardiovascular, neurologic, renal, endocrine). It may be helpful to know the specific catecholamine secreted by the tumor (epinephrine, norepinephrine, dopamine). The degree of biochemical control is based on control of blood pressure and other symptoms (tachycardia, flushing) with  $\alpha$ -blockade. Phenoxybenzamine, 10 to 20 mg/d, is the primary agent for outpatient control. Shorter-acting  $\alpha$ -adrenergic agents (prazosin, terazosin, doxazosin) may be used for long-term control of symptoms for patients with metastatic disease.  $\alpha$ -methyltyrosine may be added if symptom control is inadequate with  $\alpha$ -blockade alone. If  $\beta$ -blockade is a component of the medical regimen, it is important to know the

**Box 7****Pheochromocytoma: presurgical preparation and optimization***Diagnosis*

- Consider association with other hereditary syndromes:
  - MEN-2
  - Neurofibromatosis type 1
  - Von Hippel–Lindau syndrome
  - Osler-Weber-Rendu syndrome
  - Familial paraganglioma

*Preoperative Medical Management: Begin 10 to 14 Days Before Surgery*

- $\alpha$ -Blockade: administer with or without elevated catecholamines
  - Phenoxybenzamine (by mouth) 10 to 20 mg/d or
  - Phentolamine (intravenous) 2.5 to 5 mg bolus titrated to effect
- Alternative agents
  - Calcium-channel blockers or
  - Short-acting selective  $\alpha$ 1-blocking agents
    - Prazosin
    - Terazosin
    - Doxazosin
- Tyrosine hydroxylase blockers
  - $\alpha$ -Methyltyrosine
- $\beta$ -Blockade (only after  $\alpha$ -blockade)
  - Use for control of tachyarrhythmias or angina
- Intravascular volume expansion

indications (angina, arrhythmia, coronary artery disease). It is recommended that  $\beta$ -blockade not be instituted until adequate  $\alpha$ -blockade has been achieved to avoid unopposed  $\alpha$  activity. Medications should be continued before surgery, during surgery, and immediately after surgery. Parenteral agents (phentolamine, 2.5–5 mg every 1–2 hours) may be substituted if the oral  $\alpha$ -blocking agents are not feasible.

Evaluation for the presence or absence of cardiac disease or cardiac dysfunction is essential, because cardiomyopathy may result from the effect of chronic catechol excess, and coronary artery disease may be an unrelated comorbidity. The resting electrocardiogram and echocardiogram may be helpful in guiding perioperative management. Additional cardiac workup should be based on symptoms, signs, and risk factors. Intravascular volume deficits should be assessed and replaced up to 7 days before the scheduled endocrine or nonendocrine surgery in the patient with pheochromocytoma. Hyperglycemia may be related to catechol excess, and warrants close monitoring and management.

Carcinoids tumors originate from neuroendocrine tissues located in the lungs, thymus, or gastrointestinal tract. Carcinoids that originate in the lung are associated with corticotropin secretion and Cushing syndrome; those that originate in the gastrointestinal tract are associated with carcinoid syndrome with the secretion of serotonin,

histamine, or tachykinins. Common carcinoid syndrome symptoms are flushing and diarrhea. Right-sided cardiac valvular abnormalities (tricuspid regurgitation and pulmonic stenosis) are associated with the disease.<sup>23</sup> Flushing mimics an allergic response; hence an understanding of the patient's symptoms and presentation are essential to management, because the approach to treatment will differ based on the diagnosis. Once the diagnosis of carcinoid is established, repeated assays of 5-hydroxyindoleacetic acid are not required for surveillance before nonendocrine surgery. Octreotide (short-acting octreotide: subcutaneous 150–250  $\mu\text{g}$  3 times a day; long-acting, slow-release octreotide: intramuscular 20–30 mg once a month) is prescribed for chronic management and symptom control. If the disease is progressive or metastatic, interferon- $\alpha$  may be used for its antitumor effect. Side effects of octreotide that may affect preoperative management include hyperglycemia or hypoglycemia and bradycardia, and inhibitory effects on other pituitary thyrotropin and GH secretion. The preprocedural optimization of the patient with carcinoid syndrome requires the control of symptoms with octreotide, and the monitoring and management of its side effects.

## SUMMARY

Treatment options that reduce disease burden have allowed several endocrinopathies to be managed as chronic diseases. The current professional society consensus statements and guidelines were developed using specialist experts, current practice, consensus panels, and reviews of the existing literature. Most of these guidelines do not specifically address the care of the patient who is undergoing non-endocrine surgery. However, the principles for management are applicable to preoperative preparation of the patient presenting for surgery or other procedures. Because endocrine disorders have multisystem effects, preoperative optimization requires the recognition of the comorbidities associated with the endocrine disorder that are related to the disease itself and to its treatment. Preoperative preparation should include assessment of the course of the disease, and documentation of the therapy's medication regimen and side effects. For the practitioner managing the patient before surgery, communication and documentation of the premorbid condition and the coordination of care with those who will care for the patient during and after surgery (anesthesiologists, surgeons, hospitalists, and other internists) is essential.

## REFERENCES

1. Committee on Standards and Practice Parameters, Apfelbaum JL, Connis RT. Practice advisory for preanesthesia evaluation—an updated report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. *Anesthesiology* 2012;116(3):522–38.
2. Van Den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001;345(19):1359–67.
3. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006;354(5):449–61.
4. International Surviving Sepsis Campaign Guidelines Committee. Surviving sepsis campaign. International guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med* 2008;36(1):296–327.
5. Gu W, Pagel PS, Warltier DC, et al. Modifying cardiovascular risk in diabetes mellitus. *Anesthesiology* 2003;98(3):774–9.

6. Suleiman M, Hammerman H, Boulous M, et al. Fasting glucose is an important independent risk factor for 30-day mortality in patients with acute myocardial infarction: a prospective study. *Circulation* 2005;111(6):754–60.
7. NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009;360(13):1283–97.
8. Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence based review. *Anesthesiology* 2009;110(2):408–21.
9. Moghissi E, Korytkowski M, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Endocr Pract* 2009;15(4):1–17.
10. Joshi GP, Chung F, Vann MA, et al. SAMBA consensus statement on perioperative blood glucose management in diabetic patients undergoing ambulatory surgery. *Anesthesiology* 2010;111(6):1378–87.
11. American Diabetes Association. Standards of medical care in diabetes—2013. *Diabetes Care* 2013;36(Suppl 1):S11–66.
12. Qaseem A, Humphrey L, Sweet D, et al. Oral pharmacologic treatment of type 2 diabetes mellitus: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2012;156:218–31.
13. Kitabchi A, Umpierrez GE, Miles JM, et al. Consensus statement: hyperglycemic crises in adult patient with diabetes. *Diabetes Care* 2009;32(7):1335–43.
14. Rice MJ, Coursin DB. Continuous measurement of glucose: facts and challenges. *Anesthesiology* 2012;116(1):199–204.
15. Axelrod L. Perioperative management of patients treated with glucocorticoids. *Endocrinol Metab Clin North Am* 2003;32(2):367–83.
16. Salem M, Tainsh RE, Bromberg J, et al. Perioperative glucocorticoid coverage. A reassessment 42 years after emergence of a problem. *Ann Surg* 1994;219:416–25.
17. Marik PE, Varon J. Requirement of perioperative stress doses of corticosteroids. *Arch Surg* 2008;143(12):1222–6.
18. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocr Pract* 2012;18(6):989–1028.
19. Bahn RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Endocr Pract* 2011;17(3):456–520.
20. Melmed S, Colao A, Barkan M, et al. Guidelines for acromegaly management: an update. *J Clin Endocrinol Metab* 2009;94(5):1509–17.
21. Katznelson L, Atkinson JL, Cook DM, et al. American Association of Clinical Endocrinologists. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of acromegaly—2011 update. *Endocr Pract* 2011;17(Suppl 4):1–44.
22. Chen H, Sippel R, O'Dorisio MS, et al. The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors. *Pancreas* 2010;39(6):775–8.
23. National Comprehensive Cancer Network Guidelines. Version 1. 2012. Neuroendocrine Tumors Copyright 2013, National Comprehensive Cancer Network, Inc. All Rights Reserved..