

Adrenal Insufficiency and Other Adrenal Oncologic Emergencies

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KEYWORDS

- Adrenal insufficiency • Corticosteroids
- Aldosterone • Megestrol • Pheochromocytoma
- Hypothalamic-pituitary axis • Incidentaloma

The adrenal gland, and its endocrine function, is frequently affected by a variety of malignancies involving other organs or by their treatment. In addition, primary adrenal cancers can alter normal adrenal function and response to stress. The failure to recognize chronic or acute adrenal insufficiency or epinephrine excess can cause significant morbidity or mortality.

ADRENAL GLAND OVERVIEW

The adrenal glands are paired organs, weighing between 3 and 5 g, located at the superior poles of the kidneys, and they are well visualized by computed tomography (CT) and magnetic resonance imaging (MRI). Aldosterone, cortisol, and epinephrine are the 3 major products of the gland. Additionally, the adrenal gland is responsible for the production of small amounts of estrogen, androgen, and 2 androgen precursors. The cortex of the adrenal gland is composed of 3 layers: glomerulosa, fasciculata, and the reticularis. The glomerulosa, composing ~ 5% of the mature cortex, is responsible for aldosterone production, which has a key role in the maintenance of salt balance and blood pressure regulation. Cortisol is secreted by the fasciculata, which makes up about 70% of the cortex. Sex hormones and their precursors are products of the reticularis. Epinephrine and norepinephrine are produced by chromaffin cells located in the central zone of the gland, the medulla. Important oncologic-related adrenal disorders to be identified in the emergency department (ED) include the following: (1) inadequate cortisol production (adrenal insufficiency), (2) excess cortisol production, and (3) excess catecholamine release (pheochromocytoma).

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Regulation of Cortisol Production, the Hypothalamic-Pituitary-Adrenal Axis

Cortisol production is closely regulated by positive and negative feedback loops involving the hypothalamus, anterior pituitary, and the adrenal gland (**Fig. 1**). A number of different stressors stimulate the hypothalamus to secrete the corticotrophin-releasing hormone (CRH), which reaches the anterior pituitary via the hypophyseal portal vasculature. In response to CRH, the anterior pituitary secretes adrenocorticotrophic hormone (ACTH). ACTH stimulates cells in the fasciculata layer of the adrenal cortex, which, in turn, secrete cortisol. Cortisol is essential in the body's response to stress, impacting immune function, vascular tone, as well as lipid, protein, and carbohydrate metabolism. Via a negative feedback loop, cortisol inhibits the secretion of CRH and ACTH. Knowledge of the hypothalamic-pituitary-adrenal (HPA) axis is essential in understanding how cancer, or its treatment, may produce inadequate or excess levels of cortisol and cause the resulting syndromes.

Regulation of the Renin-Angiotensin-Aldosterone System

The production of aldosterone is frequently impaired by processes causing primary adrenal insufficiency, and hypoaldosteronism contributes to a number of the clinical findings that are observed. The regulation of aldosterone production is summarized in **Fig. 2**. Briefly, juxtaglomerular cells associated with the afferent arterioles of glomerular afferent arterioles are the primary site of renin secretion. In response to inadequate vascular volume, renin is secreted. Renin in turn converts angiotensinogen to angiotensin I, which is then converted to angiotensin II (primarily in the lungs). Angiotensin II has numerous biologic effects, one of which is the stimulation of the adrenal cortex glomerulosa layer to synthesize and secrete aldosterone. Aldosterone acts on the thick ascending loop of Henle to increase sodium reabsorption, leading to volume expansion. Decreased levels of sodium and chloride are sensed by the macula densa cells of the distal tubule (associated with inadequate vascular volume) and also stimulate renin release. Elevated sodium and chloride levels (associated with adequate vascular volume) lead to inhibition of renin secretion.

From this discussion, it is clear that in primary adrenal insufficiency, processes leading to hypoadrenalism will be associated with salt wasting and inadequate intravascular volume. The findings of dehydration, hypotension, hyponatremia, and

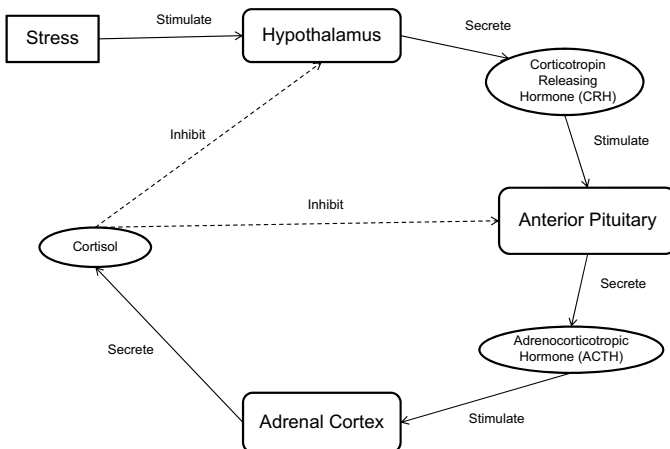


Fig. 1. The HPA axis.

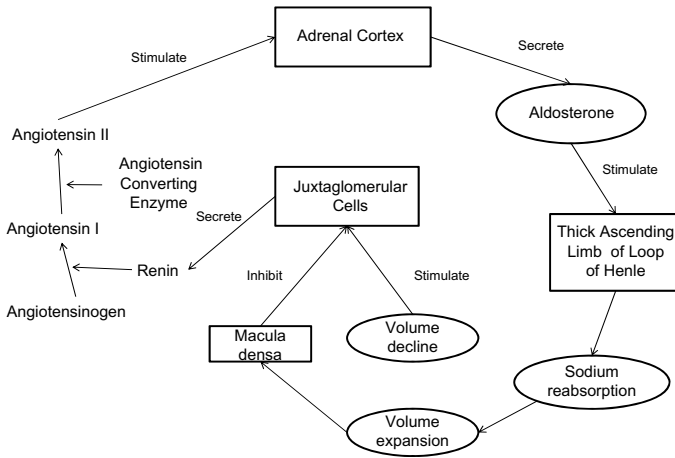


Fig. 2. Renin-angiotensin-aldosterone system.

hyperkalemia may occur. In addition, primary adrenal masses with unregulated aldosterone production will lead to hypertension and hypokalemic alkalosis (Conn’s syndrome).

ADRENAL INSUFFICIENCY SYNDROMES (HYPOCORTISOLISM)

Adrenal insufficiency is a syndrome caused by inadequate amounts of cortisol caused by a variety of primary adrenal diseases and by processes affecting the HPA axis. It may be classified as either primary (diseases affecting the adrenal gland itself) or as secondary (inadequate ACTH production) leading to inadequate cortisol production. The differentiation between primary and secondary adrenal insufficiency may be suggested by an examination of the skin and serum sodium and potassium levels (Table 1). Oncologic-associated causes of adrenal insufficiency are listed in Table 2.

Presenting Signs and Symptoms of Adrenal Insufficiency

Nonspecific symptoms are typical of adrenal insufficiency and include fatigue, anorexia, abdominal complaints (nausea, vomiting, and pain), dehydration, and orthostatic hypotension. Although hyperpigmentation (particularly noticeable in non-sunlight-exposed areas) is characteristic of primary adrenal insufficiency, it is not usually present in patients with secondary adrenal insufficiency. Laboratory findings that may be present include hyponatremia, hyperkalemia, and hypoglycemia (particularly in the fasting state). However, these are found less frequently in secondary adrenal insufficiency. Anemia, lymphocytosis, and eosinophilia may be present as well. Although mild presentations are the norm, acute adrenal crisis has life-threatening

Table 1 Primary versus secondary adrenal insufficiency		
Characteristics	Primary	Secondary
Skin	Hyperpigmented (especially in non-sun-exposed areas)	Pale (not due to anemia)
Sodium levels	Low	Low or normal
Potassium levels	High	Normal

Primary Adrenal Insufficiency	Secondary Adrenal Insufficiency
Bilateral adrenal metastasis	Pituitary or hypothalamus surgery
Bilateral adrenal hemorrhage	Pituitary or hypothalamus tumors
Bilateral adrenalectomy	Pituitary hemorrhage (apoplexy)
—	Pituitary or brain irradiation
—	Discontinuation of chronic glucocorticoid therapy
—	Medications (eg, megestrol acetate)

presentations. This is particularly true in patients with underlying malignancies, in whom there is a greater risk of decompensation due to an inability to appropriately respond to any stress with cortisol production. In primary adrenal insufficiency, the signs and symptoms of hypocortisolism are also affected by the degree to which aldosterone production is reduced. Most cases of adrenal crisis occur in patients with known underlying adrenal insufficiency. In addition to the signs and symptoms discussed here, another important presentation is that of hypotension, which responds poorly to aggressive fluid resuscitation and vasopressors. Abdominal pain, weakness, loss of consciousness, and fever often confuse the diagnosis of adrenal crisis, delaying appropriate management.

Management of Adrenal Insufficiency

Key to the management of adrenal insufficiency is its early recognition, which requires a high index of suspicion. As discussed above, the symptoms and signs of adrenal insufficiency can be vague and delay its diagnosis. In both primary and secondary adrenal insufficiency, treatment centers on the replacement of cortisol, and in the case of primary adrenal insufficiency, also mineralocorticoids (**Table 3**).¹ Patients presenting with acute adrenal crisis will require admission, generally to an intensive care unit. The disposition of patients with suspected chronic adrenal insufficiency will be dependent on their presentation and underlying illnesses.

Testing for Adrenal Insufficiency

In a state of stress, a random cortisol level should be sufficient to indicate if the patient has a decreased ability to respond with increased glucocorticoid production. The level of appropriate response has been debated, although 20 µg/dL is typically accepted as the cutoff point. If the patient has a cortisol level greater than 20 µg/dL, adrenal function is generally adequate, and if it is less than 4 µg/dL, it indicates that it is deficient.⁴ Ranges, though, have been cited from 10 to 34 µg/dL.⁵ Morning cortisol levels are not particularly applicable in the ED setting.

The insulin tolerance test (ITT) is the gold standard for testing the HPA axis. Unfortunately, in very sick patients, inducing hypoglycemia is not always reasonable, as this in itself can induce an acute adrenal crisis. In the ITT, insulin is used to induce hypoglycemia, following which cortisol levels are then measured, as hypoglycemia is a potent stimulus of the HPA axis. A cortisol level greater than 18 to 25 µg/dL is generally considered to represent an adequate response.⁴⁻⁶ Blood sugar levels are usually reduced to less than 40 mg/dL, which makes the ITT impractical in the very ill, the elderly, and patients with a history of cardiac disease, seizures, or cerebrovascular disease.⁶ In addition, some patients may have an appropriate cortisol response to hypoglycemia and still have underlying adrenal insufficiency.

Table 3 Management of adrenal insufficiency	
Acute Adrenal Insufficiency (Crisis)	Chronic Adrenal Insufficiency
Pretreatment laboratory tests Electrolytes, calcium, glucose baseline cortisol, ACTH, renin, & aldosterone	Confirmed by diagnostic testing
ACTH stimulation test with cortisol level 30 min postinjection	—
Fluid resuscitation (D5 NS or NS)	—
Glucocorticoid administration Hydrocortisone 100–200 mg IV, repeat 50–100 mg IV every 6 h until confirmatory tests available Dexamethasone 6–10 mg IV (use if ACTH stimulation test is to be performed, does not interfere with cortisol-level measurement)	Glucocorticoid administration: Hydrocortisone 15–25 mg daily po or Cortisone acetate 25–37.5 mg daily po divided bid or tid Mineralocorticoid replacement (only in primary adrenal insufficiency): Fludrocortisone 0.05–0.2 mg po daily
—	Hydrocortisone “stress” dosing Minor: 30–50 mg daily Major: initially 150 mg in D5 W over 24 h & then 100 mg in next 24 h followed by taper
Admit to ICU	—

Data from Refs. 1–3.

The metyrapone test is an overnight HPA axis test that works by blocking the negative feedback inhibition of cortisol. Metyrapone inhibits the adrenal enzyme 11-hydroxylase, prevents the conversion of 11-deoxycortisol to cortisol, and causes a drop in serum cortisol. The induced drop in cortisol in a patient with an intact HPA axis should cause the pituitary to release ACTH, which stimulates the adrenal glands to increase cortisol production (demonstrated by a rise in 11-deoxycortisol).⁷ It is used infrequently as it can also precipitate an acute adrenal crisis. In addition, other drugs may affect metyrapone’s clearance, leading to errors in interpretation. The metyrapone test, however, is a useful reference test to assess other methods for determining adrenal insufficiency, such as the ACTH stimulation testing.⁸

ACTH (Cosyntropin) stimulation testing is currently the preferred test for adrenal insufficiency. Two separate doses have been validated in the literature, with uncertainty as to which is more effective.^{5,6,9} This test assesses only the ability of the adrenal cortex to respond with increased cortisol production and not of the HPA axis as a whole. In this test, either 1 μg (low dose–physiologic) or 250 μg (standard–supraphysiologic) of cosyntropin, a synthetic derivative of ACTH that acts directly on the adrenal cortex, is administered after a baseline cortisol level is drawn. A repeat cortisol level is drawn 30 minutes later. Independent of the cosyntropin dose used, either of the following 2 results is considered evidence of an appropriate adrenal response: (1) a cortisol level of 20 to 25 $\mu\text{g}/\text{dL}$ or (2) an increase of more than 9 $\mu\text{g}/\text{dL}$ above the baseline value. It has been suggested that only the peak cortisol level be used and not the change in cortisol as a basis for treatment.¹⁰ An abnormal ACTH stimulation test effectively “rules in” adrenal insufficiency, however a normal test does not completely “rule it out,” as the reported range of sensitivities of the test are 65% to 100%.¹¹

In summary, for suspected adrenal insufficiency, it is reasonable to obtain a random cortisol level and consider an ACTH stimulation test in the ED. However, therapy for adrenal insufficiency should not be delayed to wait for test results. Dexamethasone can also be used in the ED, since it does not interfere with the results of the ACTH stimulation test.

Cancer as a Cause of Adrenal Insufficiency

Although rare, patients with cancer of nearly any type can present with adrenal insufficiency. To cause adrenal insufficiency, 90% of the adrenal gland must be nonfunctional before adrenal function is detectably impaired.¹² Often this is through metastasis. The most common cancers to metastasize to the adrenals are lung, breast, and melanoma. Renal, thyroid, and colon cancer have also been known to metastasize to the adrenals. These metastases may be either unilateral or bilateral, although the larger bilateral tumors tend to be the symptomatic ones. Patients with hypoadrenalism often present with the same nonspecific symptoms frequently associated with the cancer itself, including fatigue, weakness, and weight loss. Nonspecific abdominal pain is present in 50% of these patients. A high index of suspicion must be maintained to appropriately evaluate for adrenal insufficiency in these patients and to initiate treatment in a timely fashion.

In addition to a site of metastasis, the adrenal glands can also be a primary site of cancer as well, causing acute adrenal insufficiency once the tumor has reached a critical mass. Adrenal masses are found in at least 3% of people older than 50; years at autopsy. Nearly all are nonfunctional, and 1 in 4,000 is malignant.¹³ The size of the tumor correlates with its likelihood of being a primary adrenal adenocarcinoma. One-quarter of tumors larger than 6 cm are malignant, whereas only 2% of those less than 4 cm are malignant.¹³ Patients with tumors 6 cm or larger in size tend to have poor outcomes. With regard to adrenal function, tumors larger than 3 cm tend to be hyperfunctioning, whereas smaller tumors are likely to be nonfunctional.

Tumors of the adrenal cortex may also be benign or malignant, and both may or may not be functional. The tumors that cause virilization through excess sex steroid production tend to be malignant adrenocortical carcinomas, whereas the cortisol- and aldosterone-secreting tumors tend to be benign. Those that are functional result in hypercortisolism or hyperaldosteronism. These tumors are evaluated radiologically and by assessing the appropriate hormone levels. If less than 12 cm, laparoscopic adrenalectomy is the treatment of choice for benign tumors. Complete surgical resection is the treatment of choice for stage I to III adrenocortical carcinomas. Adjuvant therapies, such as chemotherapy and radiation, may then be employed.¹¹

Cancer Treatments and Their Effects on the HPA Axis

Apart from the havoc that cancer or its adrenal metastases might wreak on a patient, treatment for cancer can cause an unending series of complications by affecting the function of the HPA axis and the adrenal glands. Commonly, cancer patients have difficulties with oral intake secondary to decreased appetite. Megestrol acetate, a synthetic progesterone-like compound, is commonly used as an appetite stimulant in these patients. It has been noted that the extended use of megestrol can cause Cushing-like symptoms, and its rapid withdrawal can precipitate acute adrenal insufficiency. Although the exact mechanism of action is unclear, megestrol appears to suppress the HPA axis through its glucocorticoid-like activity. It is incumbent, therefore, to keep the HPA axis in mind when patients currently taking megestrol, or having recently withdrawn from megestrol, present with symptoms such as fatigue, weight loss, and electrolyte disturbances.¹⁴ The duration of megestrol use does not appear

to be particularly relevant, as cortisol levels in healthy volunteers were noted to be suppressed after a single low dose.¹⁵ On the other hand, patients treated with high-dose megestrol are likely to have Cushing-like features, such as moon facies, striae, myopathy, and centripetal obesity. New-onset diabetes has been seen as well. Agonist effects are more likely to occur in those on longer courses with higher doses of megestrol.¹⁶ Symptoms of adrenal insufficiency may become clinically apparent when (1) a patient misses a dose of megestrol, leading to sudden withdrawal of glucocorticoid activity; (2) a patient experiences significant stressors (eg, infection); (3) the megestrol binds the glucocorticoid receptors, preventing more effective endogenous glucocorticoids; and (4) greater inhibition of the HPA axis compared with its ability to signal peripheral metabolic effects of glucocorticoids.¹⁶ Cancer patients may require stress dosing of steroids while on megestrol and should be counseled not to stop this medication on their own.¹⁷

Other common medications, such as opioids, can also induce adrenal insufficiency. A case report¹⁸ published in 2005 describes a patient whose HPA axis was suppressed by chronic transdermal fentanyl use. In addition, morphine has also been shown in rats to increase the levels of corticosteroid-binding globulin and thereby reducing active free corticosteroid blood levels. This may lead to immune compromise, as glucocorticoids are needed to maintain normal immune function.¹⁹

There is a large literature describing the affects of the treatment of brain cancer and brain metastasis on the HPA axis. Studies have shown neuroendocrine dysfunction years after treatment from primary brain tumors to be more common than initially postulated.²⁰ Symptoms may start subtly but can have a major effect on the quality of life.²⁰ Now that survival rates for adults with primary brain tumors are higher than those in patients in the past, there is a notable increase in neuroendocrine dysfunction in these patients, even years after treatment. The source of the dysfunction is likely at the level of the hypothalamus as opposed to the pituitary gland, since the former is more sensitive to radiation. Up to 21% of patients with nonpituitary primary brain tumors treated with irradiation will develop secondary glucocorticoid deficiency.²¹ The likelihood of developing dysfunction is dependent on the duration and intensity of the brain irradiation. At lower radiation doses, ACTH suppression is practically unheard of, especially if the primary malignancy was not a pituitary or nasopharyngeal cancer.²² Irradiation for acute lymphoblastic leukemia also places a patient at risk for subsequent neuroendocrine dysfunction.

One of the most commonly used medications in patients with cancer that affect endogenous glucocorticoid production is supplemental steroids. Steroids are often added to patients' regimens for a variety of reasons, including pain control, reduction of edema in patients with CNS malignancies, prevention of vomiting, and prevention of common allergic reactions associated with chemotherapies. They are also used as a component of treatment regimens for patients with prostate cancer, breast cancer, thymomas, as well as some hematologic malignancies. In contrast, glucocorticoids used as monotherapy or adjuvant therapy in patients with lung cancer actually decrease survival.²³ In patients with multiple myeloma, dexamethasone may induce remission in up to 40% of patients with baseline good prognostic indicators and is quite useful for patients who would be unable to tolerate more toxic marrow-suppressive agents. Steroids are also used as maintenance therapy in multiple myeloma patients.²⁴ Side effects, unfortunately, are particularly common in the elderly. Adverse effects include hyperglycemia, bacterial and fungal infections, reactivation of herpes, psychosis, hypertension, and fluid retention.

Regardless of their intended use, administration of glucocorticoids in various formulations can cause Cushing-like effects and subsequent adrenal insufficiency if the

steroid need is no longer met, with either reduction of dose, withdrawal, or increased stress on the patient. Adrenal atrophy may be caused by the negative feedback inhibition of cortisol secretion in patients receiving long-term glucocorticoid therapies.¹ Again, these patients may present to the ED with vague effects related to their underlying cancer or therapy-related complaints. The ED physician must consider adrenal insufficiency when evaluating these patients. Depending on the severity and type of the insufficiency, typical laboratory abnormalities may or may not be present.

Finally, there are particular medications that can affect cortisol levels in any sick patient in the ED. One of the most common is etomidate, an induction agent often used for rapid sequence intubation. Etomidate lowers cortisol levels and responsiveness to ACTH by inhibiting 11-beta-hydroxylase. Patients taking spironolactone, ketoconazole, and estrogens may also have lower cortisol levels or decreased responsiveness to cortisol induction by ACTH or its equivalent.²⁵

CORTISOL EXCESS

Although rarely is the diagnosis definitively made nor treatment initiated in the ED, it is important to consider cortisol excess in the appropriate clinical settings and to refer the patient for further evaluation. Patients with untreated cortisol excess have a much increased morbidity and mortality, which can be reduced by appropriate management.

The most common cause of hypercortisolism (Cushing's syndrome) in the United States is the use of exogenous glucocorticoids. If exogenous glucocorticoids as an etiology is eliminated, the remaining mechanisms (**Table 4**) may be classified as ACTH dependent (cortisol secreted in response to excess ACTH) or independent (cortisol secreted independent of ACTH stimulation).^{26,27} The most common oncologic-associated cause (70% of all nonpharmacologic cases) is ACTH secretion by a pituitary adenoma (Cushing's disease).^{26,27} The majority of remaining cases are evenly split between ACTH-secreting nonpituitary tumors (frequently lung) and cortisol-producing primary adrenal tumors.^{26,27}

Excessive cortisol causes a myriad of signs and symptoms, the most classic of which include central obesity, moon facies, deep purple striae, supraclavicular fat pad, and proximal muscle weakness. Other features are summarized in **Box 1**. It is rare, however, for patients to have all of the classic findings, and in many instances the signs and symptoms overlap with a host of other medical conditions (eg, depression, obesity, alcoholism).²⁷ A not uncommon ED presentation of patients with Cushing's syndrome is that of psychiatric illness, most often depression.²⁸ The diagnosis of Cushing's syndrome/disease is a difficult one to make on clinical grounds. In addition,

Table 4 Nonpharmacologic causes of Cushing's syndrome	
ACTH Independent	ACTH Dependent
Adrenal tumors (15%) Adrenal adenoma Adenocarcinoma	ACTH-producing pituitary tumor (70%)
Other (rare) Pigmented nodular adrenocortical disease Massive macronodular adrenocortical disease	ACTH-producing nonpituitary tumor (15%)

Data from Refs. ^{26,27}.

Box 1**Symptoms and signs of hypercortisolism**

Central obesity
Striae
Facial rounding (moon faces)
Supraclavicular fat pads
Hypertension
Hirsutism
Oligomenorrhea
Erectile dysfunction
Plethora
Muscle weakness (typically proximal)
Osteoporosis
Psychiatric illness (especially depression)
Lethargy
Acne
Bruising
Poor wound healing
Alopecia
Hyperkalemia
Glucose intolerance/diabetes mellitus

laboratory testing to confirm the diagnosis is infrequently available in a timely fashion in the ED. Fortunately, rarely does Cushing's syndrome require emergent management. It is important for the diagnosis to be considered in the ED differential diagnosis of illnesses with overlapping signs and symptoms and for this group of patients to be referred for further testing in a timely manner.

CATECHOLAMINE EXCESS***Pheochromocytoma***

Adrenal tumors may also involve the medulla, and these tend to be neuroendocrine tumors. The most known of these are pheochromocytomas, which are catecholamine-producing tumors derived from chromaffin cells. They typically present in the fourth or fifth decade of life and are typically solitary and unilateral.²⁹ Only about 10% of pheochromocytomas are malignant.²⁹ Unfortunately, the malignant potential is often not determined until the pheochromocytoma has already metastasized. Sites of metastasis include lungs, liver, lymph nodes, and bone, the latter of which bodes the best prognosis. Malignant tumors are usually larger, extra-adrenal, and associated with higher levels of catecholamines in the plasma or urine. The presence of the succinate dehydrogenase family of gene mutations is also more likely in malignant tumors.³⁰ Symptoms associated with pheochromocytomas are the direct result of elevated catecholamine levels. Typically, both norepinephrine and epinephrine are released with a predominance of norepinephrine; however, any combination of catecholamine release may be seen, with some tumors also producing dopamine.³¹ The

classic symptom triad of episodic headache, diaphoresis, and palpitations or tachycardia or 1 or more of the components of the triad have been reported in 90% of patients in some series.²⁹ In other series, 50% of patients may have sustained hypertension, and 10% to 15% may have orthostatic hypotension.²⁹ Additional symptoms may include anxiety, chest pain, weakness, and weight loss. ED management focuses on the timely referral of patients with suspicious signs and symptoms. If management of the hypertension is necessary in the ED, an alpha-blocking agent (typically phentolamine) should be initiated before the use of any beta-blocking agent, to prevent the severe hypertension associated with unopposed alpha-receptor stimulation. In addition, the ED physician should avoid medications that may cause catecholamine release (eg, opiates, histamine, sympathomimetics) or that block catecholamine reuptake (eg, tricyclic antidepressants).²⁹

No treatment has proven consistently successful in the treatment of pheochromocytomas. Surgical resection may be curative in some instances. Debulking surgery is often used for symptomatic relief, and radiation therapy, for bony metastases. Chemotherapy may be used after surgery, but complete remission is unfortunately rare (5%).¹¹

MANAGEMENT OF INCIDENTALOMAS

With ongoing improvements in imaging (particularly CT and MRI) and their ever increasing ED use, the discovery of “incidental” adrenal masses (unexpectedly found on a radiograph examination for a nonadrenal indication) and decisions about their further evaluation are common problems. Autopsy studies of patients older than 50 years of age show an incidence of adrenal masses of at least 3%. The incidence of adrenal masses (1 cm or greater) found on radiographic imaging is comparable with an incidence of about 4%. The likelihood of finding an incidentaloma increases with age. Incidentalomas are present in less than 1% of patients younger than 30 years and in approximately 7% of individuals older than 70 years.³² The etiology of the mass varies from benign to life threatening and is summarized in **Box 2**. The majority of adrenal masses are non-hypersecreting benign adenomas (~70%).^{13,32,33} In patients with known nonadrenal cancers, nearly 75% will be metastases compared with less than 1% without known malignancies.¹³ As the size of the mass increases, so does the likelihood that it is malignant. In addition, benign lesions that are hypersecreting cortisol, aldosterone, catecholamines, or sex hormones can cause substantial

Box 2

Etiology of adrenal incidentalomas

- Adrenocortical adenoma
- Adrenocortical carcinoma
- Pheochromocytoma
- Metastasis
- Other adrenal tumors
- Hematoma
- Cysts
- Infection
- Other

morbidity and mortality. As a result, all patients with newly discovered adrenal masses in the ED should be referred for further radiographic and biochemical evaluation.¹³ The main questions to be answered are (1) is the mass hypersecreting and (2) is the mass malignant?

SUMMARY

Normal function of the adrenal gland can be disrupted not only by metastases of non-adrenal cancers but also by their treatment. In addition, tumors of the adrenal gland itself can cause disease by hypersecretion of a variety of hormones, adrenal gland destruction with inadequate production of cortisol, and by metastasis to other sites. Although rare, abnormal adrenal function, especially adrenal insufficiency, should be considered in appropriate clinical settings, as failure to recognize and treat can result in significant morbidity and mortality. Adrenal "incidentaloma" is a frequent finding of abdominal radiologic studies. All patients with an unexpected adrenal mass should be referred for further evaluation.

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