TABLE 64-3 SYNDROMES OF ADRENOCORTICAL HYPERFUNCTION

STATES OF GLUCOCORTICOID EXCESS	STATES OF MINERALOCORTICOID EXCESS
Physiologic States	**Primary Aldosteronism**
Stress	Aldosterone-secreting adenoma
Strenuous exercise	Bilateral adrenal hyperplasia
Last trimester of pregnancy	Aldosterone-secreting carcinoma
Pathologic States	Glucocorticoid-suppressible hyperaldosteronism
Psychiatric conditions (pseudo-Cushing's disorders)	**Adrenal Enzyme Deficiencies**
Depression	11β-Hydroxylase deficiency
Alcoholism	17α-Hydroxylase deficiency
Anorexia nervosa	11β-Hydroxysteroid dehydrogenase type II deficiency
Panic disorders	**Exogenous Mineralocorticoids**
Alcohol and drug withdrawal	Licorice
ACTH-dependent states	Carbenoxolone
Pituitary adenoma (Cushing's disease)	Fludrocortisone
Ectopic ACTH syndrome	**Secondary Hyperaldosteronism**
Bronchial carcinoid	Associated with hypertension
Thymic carcinoid	Accelerated hypertension
Islet cell tumor	Renovascular hypertension
Small cell lung carcinoma	Estrogen administration
Ectopic CRH secretion	Renin-secreting tumors
ACTH-independent states	Without hypertension
Adrenal adenoma	Bartter's syndrome
Adrenal carcinoma	Sodium-wasting nephropathy
Micronodular adrenal disease	Renal tubular acidosis
Exogenous Sources	Diuretic and laxative abuse
Glucocorticoid intake	Edematous states (cirrhosis, nephrosis, congestive heart failure)
ACTH intake	

ACTH, Adrenocorticotropin hormone; CRH, corticotropin-releasing hormone.

TABLE 64-4 SIGNS, SYMPTOMS, AND LABORATORY ABNORMALITIES OF HYPERCORTISOLISM

FEATURE	PERCENTAGE OF PATIENTS
Fat redistribution (dorsocervical and supraclavicular fat pads, temporal wasting, centripetal obesity, weight gain)	95
Menstrual irregularities	80 (of affected women)
Thin skin and plethora	80
Moon facies	75
Increased appetite	75
Sleep disturbances	75
Nocturnal hyperarousal	75
Hypertension	75
Hypercholesterolemia and hypertriglyceridemia	70
Altered mentation (poor concentration, decreased memory, euphoria)	70
Diabetes mellitus and glucose intolerance	65
Striae	65
Hirsutism	65 (of affected women)
Proximal muscle weakness	60
Psychological disturbances (emotional lability, depression, mania, psychosis)	50
Decreased libido and erectile dysfunction	50 (of affected men)
Acne	45
Osteoporosis and pathologic fractures	40
Easy bruisability	40
Poor wound healing	40
Virilization	20 (of affected women)
Edema	20
Increased infections	10
Cataracts	5

Cushing's syndrome often have some, but not all, of the signs and symptoms discussed here. Typically, the obesity is centripetal, with a wasting of the arms and legs, which is distinct from the generalized weight gain observed in idiopathic obesity. Rounding of the face (called *moon facies*) and a dorsocervical fat pad (*buffalo hump*) may occur in obesity not related to Cushing's syndrome, whereas facial plethora and supraclavicular filling are more specific for Cushing's syndrome. Patients with Cushing's syndrome may have proximal muscle weakness; consequently, the inability to stand up from a squat or to comb one's hair can be revealing. Sleep disturbances and insomnia, hyperarousal in the evening and night, mood swings, and other psychological abnormalities are frequently seen. Cognitive dysfunction and severe fatigue are often present. Menstrual irregularities often precede other cushingoid symptoms in affected women. Patients of both sexes complain of a loss of libido, and affected men frequently complain of erectile dysfunction. Adult-onset acne or hirsutism in women could also suggest Cushing's syndrome. The skin striae observed in patients with Cushing's syndrome are violaceous (i.e., purple or dark red) with a width of at least 1 cm. Thinning of the skin on the top of the hands is a specific sign in younger adults with Cushing's syndrome. Old pictures of patients are extremely helpful for evaluating the progression of the physical stigmata of Cushing's syndrome.

Associated laboratory findings in Cushing's syndrome include elevated plasma alkaline phosphatase levels, granulocytosis, thrombocytosis, hypercholesterolemia, hypertriglyceridemia, and glucose intolerance and/or diabetes mellitus. Hypokalemia or alkalosis usually occurs in patients with severe hypercortisolism as a result of the ectopic ACTH syndrome.

Diagnosis

If the history and physical examination findings are suggestive of hypercortisolism, then the diagnosis of Cushing's syndrome can usually be established by collecting urine for 24 hours and measuring the urinary free cortisol (UFC). This test is extremely sensitive for diagnosis of Cushing's syndrome because in 90% of affected patients, the initial UFC level is greater than 50 µg/24 hours (Fig. 64-5).

The overnight dexamethasone suppression test has been widely used as a screening tool to evaluate patients who may have hypercortisolism. Dexamethasone, 1 mg, is given orally at 11:00 PM or midnight, and plasma cortisol is measured the following morning at 8:00 AM. A morning plasma cortisol level greater than 1.8 µg/dL suggests hypercortisolism. This test produces a significant number of both false-positive and false-negative results, but it is still recommended in the 2008 Endocrine Society consensus guidelines.

Cortisol is normally secreted in a diurnal manner: The plasma concentration is highest in the early morning (between 6:00 and 8:00 AM) and lowest around midnight. Most patients with Cushing's syndrome have blunted diurnal variation. Nighttime plasma cortisol values greater than 50% of the morning values are