Clinical Presentation

Both primary and secondary adrenal insufficiency are characterized by weight loss, fatigue, muscle weakness, orthostatic symptoms, nausea, vomiting, diarrhea, and abdominal pain. Biochemical abnormalities include hyponatremia, azotemia, eosinophilia, and anemia. Importantly, hyperpigmentation of the skin and hyperkalemia are seen only with primary adrenal insufficiency, not with ACTH deficiency.

Diagnosis and Differential Diagnosis

The gold standard for diagnosis of secondary adrenal insufficiency has been an insulin tolerance test. The test is contraindicated in elderly patients and in those with a history of seizures, cardiovascular disease, or cerebrovascular disease. A safer test is an 8 AM fasting rapid ACTH stimulation test. This test measures the cortisol response to synthetic ACTH or cosyntropin. ACTH and cortisol levels are measured at baseline, followed by cortisol levels at 30 and 60 minutes. An 8 AM cortisol level of less than 5 µg/dL suggests adrenal insufficiency. A peak plasma cortisol level higher than 18 to 20 µg/dL is considered a normal response.

Treatment

Glucocorticoid replacement therapy in the form of hydrocortisone (10 mg in AM and 5 mg in PM) or prednisone (5 to 7.5 mg/day) should be initiated. Patient education regarding stress dosing of steroids is important. Mineralocorticoids are usually not needed in patients with central adrenal insufficiency.

ACTH-Secreting Pituitary Tumors (Cushing's Disease)

Definition and Epidemiology

ACTH-secreting pituitary tumors (by definition, Cushing's disease) account for about 80% of the cases of Cushing's syndrome; they are usually microadenomas. There is a female preponderance (female-to-male ratio, about 3 : 1).

Pathology

The chronic stimulation by excessive ACTH causes simple diffuse hyperplasia of the bilateral adrenal glands or sometimes multinodular hyperplasia, both leading to excessive cortisol production.

Clinical Presentation

Signs and symptoms of Cushing's disease are related to the hypercortisolism and include central obesity, hirsutism, facial plethora, violaceous striae, supraclavicular and dorsocervical fat pads, and muscle weakness (Fig. 62-2). Additional manifestations of Cushing's disease are type 2 diabetes mellitus, hypertension, dyslipidemia, osteoporosis, and hypogonadism.

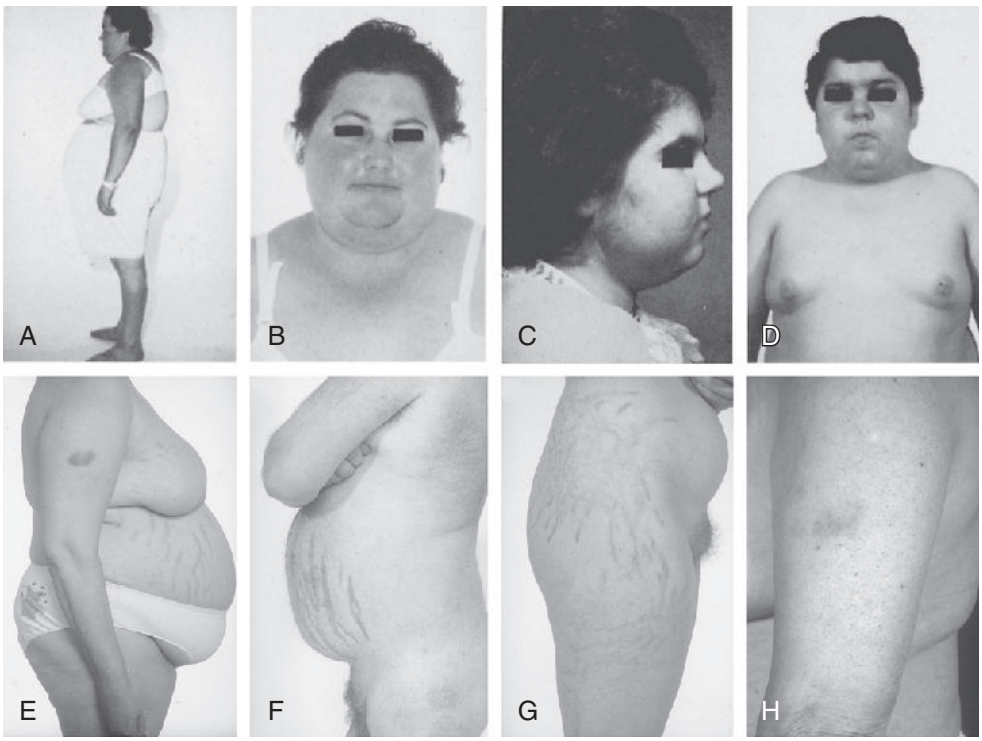

FIGURE 62-2 Clinical features of Cushing's syndrome. **A,** Centripetal and some generalized obesity and dorsal kyphosis in a 30-year-old woman with Cushing's disease. **B,** Moon facies, plethora, hirsutism, and enlarged supraclavicular fat pads in the same woman as in **A**. **C,** Facial rounding, hirsutism, and acne in a 14-year-old girl with Cushing's disease. **D,** Central and generalized obesity and moon facies in a 14-year-old boy with Cushing's disease. Typical centripetal obesity with livid abdominal striae in a 41-year-old woman **(E)** and a 40-year-old man **(F)** with Cushing's disease. **G,** Striae in a 24-year-old patient with congenital adrenal hyperplasia treated with excessive doses of dexamethasone as replacement therapy. **H,** Typical bruising and thin skin of a patient with Cushing's disease. In this case, the bruising has occurred without obvious injury. (From Larsen PR, Kronenberg H, Melmed S, et al: Williams Textbook of Endocrinology, ed 10, Philadelphia, 2003, Saunders.)