Adrenal Causes of Hypertension

**Normal pituitary-adrenal axis.** Corticotropin-releasing factor (CRF) acts to stimulate the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary. ACTH then stimulates the adrenal zona fasciculata and zona reticularis to synthesize and release cortisol (see Figs. 4-2 and 4-3). The increased levels of cortisol feed back to suppress additional release of ACTH. As shown in Figure 4-4, ACTH and cortisol have circadian patterns.

**Pituitary Cushing’s disease.** Pituitary Cushing’s disease results from excessive production of adrenocorticotropic hormone (ACTH), typically owing to a benign adenoma. Excess ACTH stimulates both adrenals to produce excessive amounts of cortisol and results in bilateral adrenal hyperplasia. The increased cortisol production does not suppress ACTH release, however, because the pituitary tumor is unresponsive to the normal feedback suppression of increased cortisol levels. The diagnosis usually is made by demonstration of elevated levels of ACTH in the face of elevated cortisol levels, particularly in the afternoon or evening, representing loss of the normal circadian rhythm (see Fig. 4-4). Radiographic studies of the pituitary (computed tomographic scan and magnetic resonance imaging) will likely demonstrate the source of increased ACTH production. When the pituitary is the source, surgery and irradiation are therapeutic options.
4.12 Hypertension and the Kidney

**SCREENING TESTS FOR CUSHING’S SYNDROME**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated pm serum cortisol</td>
<td>~75</td>
<td>~60</td>
</tr>
<tr>
<td>Elevated urinary 17-hydroxy corticosteroids</td>
<td>&gt;90</td>
<td>~60</td>
</tr>
<tr>
<td>Elevated urinary free cortisol</td>
<td>&gt;95</td>
<td>&gt;95</td>
</tr>
</tbody>
</table>

**FIGURE 4-23**
Screening tests for Cushing’s syndrome. Whereas elevated evening plasma cortisol levels typically indicate abnormal circadian rhythm, other factors such as stress also can cause increased levels late in the day. Urinary levels of 17-hydroxy corticosteroids may be increased in association with obesity. In such cases, repeat measurement after a period of dexamethasone suppression may be required to distinguish this form of increased glucocorticoid excretion from Cushing’s syndrome. The measurement of urinary-free cortisol is the most sensitive and specific screening test.

**FIGURE 4-22**
Ectopic etiology of Cushing’s syndrome. Rarely, Cushing’s syndrome may be due to ectopic production of adrenocorticotropic hormone (ACTH) from a malignant tumor, often in the lung. In such cases, hypercortisolism is associated with increased levels of ACTH-like peptide; however, no pituitary lesions are found. Patients with ectopic Cushing’s syndrome often are wasted and have other manifestations of malignancy.

**FIGURE 4-24**
Algorithm for differentiation of Cushing’s syndrome. The first step in the differentiation of Cushing’s syndrome after diagnosing hypercortisolism is measurement of plasma adrenocorticotropic hormone (ACTH) levels. Typically, these should be reduced after the morning hours (see Fig. 4-4). In pituitary Cushing’s disease and ectopic forms of Cushing’s syndrome, elevated values are observed, especially in the afternoon and evening. The next step in differentiation is an anatomic evaluation of the pituitary. When no abnormality is found, the next step is a search for a malignancy, typically in the lung. The finding of low ACTH levels points to the adrenal as the source of excessive cortisol production, and anatomic studies of the adrenal are indicated. CT—computed tomography; MRI—magnetic resonance imaging.
Adrenal Causes of Hypertension

Catecholamines

Synthesis, actions, and metabolism of catecholamines. Depicted is the synthesis of catecholamines in the adrenal medulla [9]. Epinephrine is only produced in the adrenal and the organ of Zuckerkandl at the aortic bifurcation. Norepinephrine and dopamine can be produced and released at all other parts of the sympathetic nervous system. The kidney is the primary site of excretion of catecholamines and their metabolites, as noted here. The kidney also can contribute catecholamines to the urine. The relative contributions of norepinephrine and epinephrine to biologic events is noted by the plus signs. BMR — basal metabolic rate; CNS — central nervous system; NEFA — nonesterified fatty acids; VMA — vanillylmandelic acid.