Primary renal disease can produce hypertension, but the exact mechanism is unknown. Up to 70% of patients with chronic pyelonephritis have elevated BP. Local ischemia within the kidney is suspected as the cause of hypertension. Some authors suggest local microvascular renal disease as the final common pathway underlying essential hypertension.[17] Hypertension in patients with nonspecific glomerulonephritis may result from arteriolar lesions producing ischemia at the level of the individual nephron. With the exception of renin-secreting renal tumors, the exact cause of hypertension associated with the various nephropathies is unknown.

### Arterial Disease

Abnormalities of the large arteries can also produce hypertension. Although uncommon, coarctation of the aorta is an important cause of secondary hypertension, and early surgical intervention can greatly improve the patient's prognosis.[21] The triad of upper extremity hypertension, a systolic murmur best heard over the back, and delayed femoral pulses should alert the examiner to the diagnosis of coarctation. Hypertension appears to result from the combined effects of mechanical obstruction and activation of the renin-angiotensin system.[22] Early diagnosis of coarctation is important because surgical repair results in a consistent and sustained lowering of BP. In adults, renal artery stenosis is an important cause of accelerated onset of significant hypertension, and renal artery ultrasonography or angiography is advisable (on an ambulatory basis) for patients with this type of onset of disease.

Loss of elasticity in the larger arteries associated with the aging process produces systolic hypertension as well as elevations in pulse pressure. Arteriosclerosis from the deposition of collagen and smooth muscle hypertrophy plays a major role in the age-dependent stiffness of the central vasculature. Previously, elevated systolic pressure was not considered significant and frequently was not treated. The current literature strongly suggests that isolated systolic hypertension is associated with an increased risk of stroke, heart disease, and renal failure and should be treated. The cause of reduced elasticity in the arteries associated with isolated systolic hypertension has not been fully determined. Endothelial dysfunction that develops over time with both aging and hypertension may play a critical role in this process. Other factors that decrease central vascular compliance include high dietary salt intake, tobacco use, elevated homocysteine levels, and diabetes.

### Glucocorticoids

Excessive glucocorticoids are associated with hypertension, and the most common cause is iatrogenic steroid therapy. Endogenous overproduction is rare and results from excessive adrenocorticotropic hormone (ACTH) production by a pituitary tumor, ectopic ACTH production by a nonpituitary tumor, or glucocorticoid production by tumors of the adrenal cortex. These patients show other signs and symptoms of excessive glucocorticoids, including centripetal fat distribution, striae, easy bruising, muscular weakness, and poor healing. The hypertension associated with hyperadrenalism is usually not severe and can be controlled by treating the underlying disease process.

### Thyroid and Parathyroid Disease

Both hyper- and hypothyroidism are associated with elevations in BP. In thyroid storm, patients are usually hypertensive and tachycardic, and beta-blockade is a mainstay of the acute management. Patients with hypothyroidism also present with hypertension as well as the other characteristic findings. Treatment of the hypothyroidism usually results in correction of the hypertensive state. Hypertension with hypercalcemia suggests hyperparathyroidism, which is another rare secondary cause of hypertension.

### Sleep Apnea

Both obstructive and central forms of sleep apnea are associated with hypertension. Apnea itself is associated with a significant increase in BP. Approximately 50% of patients with sleep apnea have daytime hypertension, but many have other risk factors for hypertension, such as obesity or alcohol consumption. Studies suggest that treatment of nocturnal hypoventilation may improve daytime BPs.[23,24]

### Pheochromocytoma

Pheochromocytomas are responsible for less than 1% of cases of hypertension. More than 90% of these patients are curable with early diagnosis. Pheochromocytomas produce catecholamines and arise from cells of the sympathetic nervous system. The most common site is the adrenal medulla. Patients with neurofibromatosis (von Recklinghausen's disease) have an increased incidence of pheochromocytoma. Pheochromocytoma, medullary carcinoma of the thyroid, and parathyroid adenomas form the triad of multiple endocrine neoplasia (adenomatosis), type 2.

The characteristic feature of pheochromocytoma is paroxysms of hypertension associated with palpitations, tachycardia, malaise, apprehension, and sweating. Many patients have a persistently elevated BP interspersed with episodes of greater hypertension that occur sporadically and vary greatly in severity, frequency, and duration. These episodes may be related to physical and emotional stress, eating, position, or even micturition. A prodrome of apprehension and nonspecific abdominal pain progressing to headache, palpitations, and angina may be seen. Because of the episodic nature of this syndrome, the patient is often dismissed with a diagnosis of hyperventilation syndrome or anxiety. An excessively elevated BP associated with these symptoms is enough to suggest a pheochromocytoma. Patients may also display increased BP when treated with beta-blocking agents (beta-blockers).

The diagnosis is confirmed with elevated urinary levels of catecholamines, metanephrines, and vanillylmandelic acid,[25] usually to more than twice the normal levels. Treatment consists of alpha-blockade to control hypertension and subsequent beta-blockade for the control of cardiac dysrhythmias. After the hypertension is adequately controlled, the tumor should be surgically removed.

### Other Causes

Eating foods that contain large amounts of *tyramine* can cause episodic hypertension (Box 82-1). Tyramine causes release of norepinephrine stored in nerve endings. This response is normally transient; tyramine is rapidly destroyed by monoamine oxidase. Problems arise if a patient is being treated with a monoamine oxidase inhibitor (MAOI), which protects tyramine from destruction. Relatively small amounts of tyramine can cause severe and prolonged hypertension. A number of therapeutic agents can also induce a hypertensive crisis in patients taking MAOIs. These include meperidine, the amphetamines, ephedrine, reserpine, guanethidine, and tricyclic antidepressants. The hypertension can be controlled by using an alpha-blocking agent (alpha-blocker) such as phentolamine.