The autonomic nervous system, especially through the cranial parasympathetic and lumbosacral sympathetic outflow, is closely involved in the beat-to-beat control of systemic blood pressure, heart rate, and the regional blood supply to skeletal muscle and vital organs. It is of major importance in ensuring adequate tissue perfusion, in maintaining supplies of oxygen and nutrients, and in transporting metabolic end-products in response to the demands of varying situations. It accomplishes these actions through a complex system of pathways that involves the brain and spinal cord, preganglionic and postganglionic pathways, and synapses at the target organs; the immense flexibility and capability of the autonomic nervous system are dependent on intricate pathways that may be damaged in a variety of conditions that affect one or more sites with the brain, spinal cord, or periphery (Fig. 88.1). A key component is the baroreflex pathway, an exquisitely sensitive mechanism that provides beat-by-beat blood pressure control (Fig. 88.2). This chapter discusses the classification of autonomic disorders that affect the cardiovascular system, and describes the main clinical manifestations, tests of autonomic dysfunction, and features of key major autonomic disorders. There is an emphasis on postural (orthostatic) hypotension as it is a cardinal feature of many autonomic disorders. It is now recognized that a number of factors in daily life, such as food ingestion and exercise, can themselves cause hypotension and thus worsen postural hypotension. The pressor effect of water ingestion in autonomic failure recently has been recognized, and has been introduced in the management of postural hypotension. There have been advances in the evaluation and management of neurally mediated syncope and the postural tachycardia syndrome. These are discussed, along with various advances in our understanding of how the autonomic nervous system controls cardiovascular function in humans.

Classification of Autonomic Dysfunction

Autonomic disorders may result in localized or generalized dysfunction. Examples include primary disorders where there is no clear etiologic factor (e.g., multiple system atrophy, synonymous with the Shy-Drager syndrome) and secondary disorders associated with a clearly defined lesion (e.g., spinal cord lesions), disease (e.g., diabetes mellitus), or a specific biochemical deficit (e.g., dopamine β-hydroxylase deficiency) (Table 88.1). A wide variety of drugs, toxins, and chemicals result in autonomic dysfunction by their direct effects or by causing a neuropathy. A separate category includes neurally mediated syncope in which there is an intermittent autonomic abnormality, often associated with specific events (Table 88.2). The postural tachycardia syndrome is a relatively recently described disorder with orthostatic intolerance without postural hypotension.

Autonomic dysfunction often results in diminished activity leading to hypotension and bradycardia; the reverse, overactivity, also may occur, causing hypertension and tachycardia. In some disorders, such as neurally mediated syncope, parasympathetic overactivity and sympathetic underactivity may occur simultaneously.

Clinical Manifestations

Cardiovascular Features

Autonomic dysfunction can affect the regulation of blood pressure and heart rate and impair regional vascular control mechanisms.

Postural Hypotension

Postural hypotension is a cardinal feature of sympathetic vasoconstrictor failure (Fig. 88.3). It often provides the first clue to an underlying diagnosis of autonomic failure. It is defined as a fall in systolic blood pressure of more than 20 mm Hg or in diastolic blood pressure of more than 10 mm Hg, on either standing upright or on head-up tilt to 60 degrees for 3 minutes. Normally there is no fall in blood pressure on head-up postural change. The fall in blood pressure usually is associated with symptoms of hypoperfusion to various organs, especially to those above the heart, such
as the brain\textsuperscript{7} (Table 88.3). Symptoms arising from cerebral hypoperfusion often are the reason for requesting medical advice. They are precipitated by sitting or standing, are relieved by lying flat, and may vary in the same individual at different times. Their magnitude may be independent of the fall in blood pressure. With time symptoms of cerebral hypoperfusion often are reduced, and this may be due to improved cerebrovascular autoregulation.

Common symptoms of cerebral hypoperfusion include dizziness and visual disturbances; these usually but not necessarily precede loss of consciousness (syncope, fainting). Cognitive deficits and prolonged reaction times have been recorded in subjects with moderately hypotension,\textsuperscript{8} and this may apply to subjects with postural hypotension; these deficits are likely to resolve when the blood pressure is restored. Symptoms of postural hypotension often are worse when getting out of bed in the morning and may be enhanced by a variety of stimuli in daily life, ranging from food ingestion and modest amounts of alcohol, to mild exercise and a raised environmental temperature (Table 88.4). Straining during micturition and bowel movements that commonly are affected in autonomic failure may induce symptoms. These stimuli presumably raise intrathoracic pressure, result in a Valsalva-like maneuver and thus lower blood pressure. Many subjects recognize the association between postural change and symptoms of cerebral hypoperfusion and therefore sit down, lie flat, or assume postures such as squatting or stooping. Syncope may occur rapidly if the blood pressure falls precipitously; this may be similar to a “drop” attack.

Syncope may result in injury. Seizures occasionally occur, especially if cerebral hypoxia is prolonged. A variety of drugs, ranging from sublingual glyceryl trinitrate to those

\textbf{FIGURE 88.1.} Parasympathetic and sympathetic innervation of major organs.\textsuperscript{2}

\textbf{FIGURE 88.2.} Relationship between spontaneous fluctuations of blood pressure and muscle-nerve sympathetic activity [left] recorded in right peroneal nerve. The baroreceptor reflex accounts for the pulse synchrony of nerve activity and the inverse relationship to blood pressure fluctuations. Asterisk indicates diastolic blood pressure fall due to sudden atrioventricular [AV] block. Stippling indicates corresponding sequences of bursts and heartbeats.\textsuperscript{3}