manifest with autonomic symptoms because emotional and autonomic centers are closely linked in the limbic system.

For a deeper discussion of these topics, please see Chapter 420, "Peripheral Neuropathies," Chapter 188, "Amyloidosis," and Chapter 47, "Mechanisms of Immune-Mediated Tissue Injury," in Goldman-Cecil Medicine, *25th Edition.*

CLINICAL PRESENTATION

Clinical manifestations of autonomic disorders vary according to which nerves are involved and how severely. Autonomic signs and symptoms may be benign or serious, paroxysmal or continuous, or localized or generalized, and they may represent hypofunction or hyperfunction.

Afferent autonomic lesions that separate central autonomic nuclei from incoming information needed to gauge an appropriate response may cause excessive or erratic autonomic outflow. An example of afferent dysautonomia is the volatile hypertension in carotid arterial baroreceptor failure after irradiation to treat laryngeal carcinoma. Spinal cord injuries above the level of sympathetic outflow at T5 can cause autonomic dysreflexia, a condition of paroxysmal sympathetic surges with hypertension, diaphoresis, flushing, and headache. Catastrophic brain disorders such as subarachnoid hemorrhage, trauma, or hydrocephalus may also cause autonomic storms if hypothalamic circuits are released from cortical inhibition.

More common are efferent autonomic lesions, which cause failure of outflow to neuroeffector junctions, resulting in inadequate excitatory or inhibitory autonomic responses. An example of efferent dysautonomias is autonomic peripheral neuropathy, which may accompany distal sensory loss and decreased Achilles tendon jerks.

Adrenergic failure impairs the cardiac and peripheral vascular response needed to maintain blood pressure during orthostatic stress. Typical symptoms of adrenergic failure include lightheadedness or fatigue on standing that is relieved by sitting.

Vagal failure impairs cardiac parasympathetic tone that may protect against arrhythmogenic sympathetic activity. Patients have a fixed heart rate that does not vary with respiration.

Sudomotor failure with extensive anhidrosis may coexist with tonic pupils and areflexia (i.e., Ross syndrome), and it can increase the risk of heat exhaustion or heat stroke. A dramatic example of regional sudomotor failure is harlequin syndrome, in which hemifacial cutaneous sympathetic denervation divides the pale and dry denervated half of the face from the intact half that flushes red in response to heat stress. Horner's syndrome (i.e., unilateral ptosis, miosis, and anhidrosis) may be identified.

The clinical hallmark of generalized autonomic failure is severe orthostatic hypotension without pulse acceleration. In at least one half of patients, it is accompanied by supine and nocturnal hypertension, a reversal of the normal diurnal decrease in blood pressure during sleep. In addition to vagal and sudomotor failure, patients with generalized autonomic failure may have constipation, gastroparesis, bladder dysfunction, male erectile dysfunction, dry mouth, or dry eyes. Some have postprandial hypotension, in which a large meal high in carbohydrate content causes a reduction in blood pressure.

One of the most severe autonomic disorders is multiple system atrophy, which is a sporadic, progressive, ultimately fatal neurodegenerative disorder in which autonomic failure occurs in combination with parkinsonism or cerebellar ataxia. Bladder hypotonia with overflow incontinence and nocturnal respiratory stridor may occur. The parkinsonian phenotype (i.e., Shy-Drager syndrome) tends to respond poorly to levodopa. Orthostatic hypotension is also common in Lewy body disorders such as Parkinson's disease. Pure autonomic failure consists of widespread autonomic failure without other neurologic features.

In contrast to autonomic failure, neurally mediated syncope occurs in patients with a functioning autonomic nervous system in which there is a reversal of normal autonomic outflow. Prodromal features typically include pallor, sweating, nausea, abdominal discomfort, mydriasis, increased respiratory rate, and cognitive slowing, which may progress to transient loss of consciousness if the patient continues in an upright posture. Withdrawal of peripheral sympathetic vasomotor tone (i.e., vasodepressor syncope) or an increase in parasympathetic tone (i.e., vasovagal syncope) causes a fall in blood pressure, heart rate, and cerebral perfusion.

Orthostatic intolerance refers to a heterogeneous group of conditions in which patients have difficulty sustaining the autonomic outflow needed to maintain blood pressure during the gravitational stress of prolonged standing. Some patients experience a gradual decline in blood pressure, but others experience an abnormal increase in heart rate without a drop in blood pressure.

For a deeper discussion of these topics, please see Chapter 62, "Approach to the Patient with Suspected Arrhythmia," Chapter 67, "Arterial Hypertension," Chapter 136, "Disorders of Gastrointestinal Motility," and Chapter 409, "Parkinsonism," in Goldman-Cecil Medicine, *25th Edition.*

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

A careful history and discerning physical examination are essential for reaching a diagnosis. The astute clinician inquires about the time course of symptoms and the circumstances that provoke or modify them. How long have they been present? Are they stable, improving, or worsening? Do they occur consistently or episodically? Orthostatic disorders are typically worse in the early morning, in heat, and after physical exercise or a large meal. How well the patient tolerates standing in line or taking a warm shower are helpful clues to identifying orthostatic intolerance.

Physical signs of autonomic dysfunction may include pupillary asymmetry or sluggishness, ptosis, or mucosal dryness. An acutely distended bladder may be suspected by percussion. Asymmetrical sweating may be visible or palpable.

The most important part of the examination, but one that is frequently omitted, is measurement of orthostatic blood pressure (Fig. 110-1). Blood pressure and heart rate should be assessed when the patient is resting supine and again after standing for 1 to 3 minutes or longer. Correlation with symptoms is key. Patients with orthostatic hypotension may appear less alert, or they may shift weight from one leg to the other to improve venous return, lower the head to bring the cerebral circulation closer to the level