110

Autonomic Nervous System Disorders

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DEFINITION AND EPIDEMIOLOGY

The autonomic nervous system reaches throughout the body and governs all visceral activity. Its central network and peripheral sympathetic and parasympathetic divisions integrate complex organ functions, maintain internal homeostasis in response to environmental change, modulate the flight-or-fight physiologic response to stress, and enable circulation, digestion, and procreation.

Benign dysautonomias are common. Neurally mediated syncope and situational reflex syncope in response to emotional distress, carotid sinus stimulation, micturition, defecation, coughing, straining, or other factors occur in about 20% of people during a lifetime and account for 1% to 3% of all emergency room visits. Hyperhidrosis of the palms and soles affects about 1% of the population. Anhidrosis can contribute to increased mortality rates during severe heat stress.

One of the most disabling manifestations of autonomic failure is orthostatic hypotension, the prevalence of which increases with age, physical inactivity, and in diseases that impair sympathetic adrenergic nerves. Orthostatic hypotension affects about 5% to 20% of the elderly.

Diabetes mellitus is the most common cause of autonomic neuropathy in industrialized nations. About 30% of diabetics develop autonomic neuropathy, and symptomatic orthostatic hypotension occurs in 5% of patients. Other features of autonomic neuropathy include constipation in 40% to 60% of diabetics, gastroparesis in 20% to 40%, bladder dysfunction in 30% to 80%, and erectile impotence in more than 30% of men.

For a deeper discussion of these topics, please see Chapter 25, "Common Clinical Sequelae of Aging," and Chapter 229, "Diabetes Mellitus," in Goldman-Cecil Medicine, *25th Edition.*

PATHOLOGY

Many brain, spinal cord, peripheral nerve, and systemic disorders that impair autonomic nerves can cause autonomic dysfunction or failure. They include a wide range of degenerative, traumatic, cerebrovascular, autoimmune, genetic, metabolic, toxic, and pharmacologic conditions.

Small-caliber peripheral autonomic nerves are unmyelinated or thinly myelinated, and small-fiber peripheral neuropathies that cause distal sensory loss may also involve sympathetic or parasympathetic nerves. Diabetic autonomic neuropathy results from microvascular damage to autonomic nerves. Several hereditary, infectious, metabolic, toxic, and drug-induced sensory and autonomic neuropathies are recognized causes.

Accumulation of abnormal proteins distinguishes some of the degenerative dysautonomias. Oligodendroglial cytoplasmic inclusions composed of aggregates of misfolded α-synuclein are pathognomonic of multiple system atrophy. Abnormally folded sympathetic neuronal accumulation of α-synuclein occurs in Lewy body disorders such as Parkinson's disease. Peripheral autonomic nerve deposition of β-pleated sheet amyloid protein causes a severe autonomic neuropathy, which is frequently seen in primary amyloidosis, immunoglobulin light chain–associated disease, and hereditary amyloidosis, although rarely in reactive amyloidosis.

Other dysautonomias have an autoimmune basis. Autonomic instability has long been recognized in Guillain-Barré syndrome, which is an acute inflammatory, demyelinating polyradiculoneuropathy associated with antiganglioside antibodies (e.g., anti-GM_1, anti-GM_3). The list of autoimmune autonomic neuropathies includes acute autonomic ganglionopathy; patients with acute pandysautonomia have antibodies against the nicotinic acetylcholine receptor in autonomic ganglia, which is sometimes associated with lung cancer or thymoma. Additional paraneoplastic autonomic neuropathies include those associated with antineuronal nuclear antibody type 1 (i.e., ANNA-1 or anti-Hu) and antibodies against collapsing response mediator proteins (i.e., CRMP-5 or anti-CV2). Lambert-Eaton myasthenic syndrome is associated with antibodies to voltage-gated calcium channels. Antibodies to voltage-gated potassium channels cause autoimmune neuromyotonia and dysautonomia with hyperhidrosis and orthostatic intolerance.

Pharmacologic agents frequently alter autonomic function. Diuretics, sympatholytic drugs, α-adrenoreceptor blockers, and vasodilators can cause or contribute to orthostatic hypotension. Anticholinergics and carbonic anhydrase inhibitors decrease sweating, whereas opioids and selective serotonin reuptake inhibitors increase sweating. Opioids slow intestinal transit. Anticholinergics, tricyclic antidepressants, and antihistamines may cause urinary retention.

Functional dysautonomias are medical conditions in which autonomic function is impaired in the absence of a known structural neurologic deficit. Some psychological disorders may