Autonomic Dysfunction

Autonomic dysfunction is a prominent feature of Fabry's disease, commonly manifested by hypohidrosis, acral paresthesias, and altered intestinal motility.

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Related terms:

Parkinsonism, Diabetes Mellitus, Diagnosis, Syndrome, Pain, Symptom, Blood Pressure, Orthostatic Hypotension

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Autonomic Failure

E.M. Garland, D. Robertson, in Encyclopedia of Neuroscience, 2009

Autonomic Dysfunction

The clinical features of autonomic dysfunction are pervasive, involving the cardiovascular, gastrointestinal, urogenital, thermoregulatory, sudomotor, and pupillomotor systems. Much of the testing evaluates the integrity of the cardiovascular reflexes. Under normal conditions, cardiovascular reflexes act through the autonomic nervous system to maintain blood pressure and cerebral perfusion at appropriate levels. For example, when stretch or baroreceptors detect a decrease in blood pressure, they relay this information to the central nervous system, which decreases parasympathetic tone and increases sympathetic outflow. Increases in norepinephrine (NE) secretion and peripheral resistance restore blood pressure and provide adequate cerebral perfusion. Disturbances in one or several parts of this reflex arc may result in syncope, a sudden, transient loss of consciousness with spontaneous recovery that may be associated with hypotension, bradycardia (reduced heart rate), and loss of postural tone. Conservative estimates suggest that 30% of the general population has experienced at least one syncopal spell and that syncope is responsible for over 1% of hospital admissions. Infrequently, syncope may be a sign of impaired cardiovascular reflexes resulting from autonomic failure.

Disorders of autonomic failure include central neurodegenerative diseases such as multiple-system atrophy (MSA), primary peripheral autonomic nervous system degeneration (as in autonomic neuropathy or pure autonomic failure (PAF)), and congenital diseases such as familial dysautonomia (FD) and dopamine β-hydroxylase (DBH) deficiency. Patients with severe autonomic failure experience profound hypotension either after assuming the upright position or after food consumption (orthostatic and postprandial hypotension, respectively). In baroreflex failure, exaggerated blood pressure and heart rate fluctuations are exacerbated by emotional or physical stress, whereas patients with postural tachycardia syndrome (POTS) endure orthostatic symptoms and enhanced increases in heart rate with standing. Although Parkinson's disease (PD) is primarily a disorder of motor control, cardiac sympathetic dysregulation has been demonstrated and symptoms of autonomic failure occur in 20–50% of patients. Other systemic illnesses, such as diabetes and amyloidosis, may disturb autonomic function.

Disorders of the Autonomic Nervous System

Horacio Kaufmann, Italo Biaggioni, in Brocklehurst's Textbook of Geriatric Medicine and Gerontology (Seventh Edition), 2010

Chronic autonomic failure

Autonomic failure is divided into primary and secondary forms. Primary autonomic failure is caused by a degenerative process affecting central autonomic pathways (multiple system atrophy [MSA]), or peripheral autonomic neurons (pure autonomic failure). Secondary autonomic failure results from destruction of peripheral autonomic neurons in disorders, such as diabetes, amyloidosis, and other neuropathies, and very rarely by an enzymatic defect in catecholamine synthesis (dopamine β-hydroxylase deficiency). In chronic autonomic failure, orthostatic hypotension and syncope are caused by impaired vasoconstriction and reduced intravascular volume. Vasoconstriction is deficient because of reduced baroreflex-mediated norepinephrine release from postganglionic sympathetic nerve terminals and low circulating levels of angiotensin II caused by impaired secretion of renin.[68] In patients with autonomic failure and central nervous system dysfunction (i.e., MSA), impaired endothelin and vasopressin release also contribute to deficient vasoconstriction in the standing position.[63,69]

Peripheral Nerve Disorders

Harutoshi Fujimura, in Handbook of Clinical Neurology, 2013

Autonomic dysfunction

Autonomic dysfunction occurs in approximately two-thirds of patients. It is a common and sometimes serious complication in GBS (Singh et al., 1987; Winer et al., 1988; Winer and Hughes, 1988; Moulin et al., 1997; Zochodne, 1994). The sympathetic and parasympathetic failure or inappropriate activity results in various types of cardiac arrhythmias, blood pressure fluctuations, abnormal hemodynamic responses to drugs, sweating abnormalities, pupillary abnormalities, and bladder and bowel dysfunction.

Autonomic dysfunction is usually regarded as of minor clinical importance, but life-threatening cardiovascular complications may develop. Three to ten percent of patients with GBS die, and in some of these patients the cause is likely to be (sudden) autonomic failure (Winer et al., 1988). Recognition of autonomic dysfunction is important. Possible development of serious autonomic failure must be monitored continuously in every patient; however, this is often difficult (Hughes et al., 2005). It may be noted that potentially serious bradyarrhythmias, ranging from bradycardia to asystole, are found not only in severely disabled patients, but also in patients who are still able to walk (Flachenecker et al., 2000). Application of a transcutaneous pacemaker or administration of atropine, vasoactive medication, and morphine derivatives may be considered when necessary.

Autonomic Nervous System

Horacio Kaufmann, David S. Goldstein, in Handbook of Clinical Neurology, 2013

Introduction

Autonomic dysfunction occurs commonly in patients with Parkinson disease (PD). Indeed, the original report by James Parkinson in 1817 noted prominent symptoms of constipation and urinary incontinence. The well-known movement disorder usually dominates the clinical picture and has occupied the attention of clinicians and researchers. Nevertheless, a substantial minority of parkinsonian patients have severe and disabling symptoms of autonomic impairment, several of which are treatable.

Autonomic disturbances in PD can manifest as dysphagia, constipation, urinary urgency, incontinence, erectile dysfunction, orthostatic and postprandial hypotension, dyshidrosis, and impaired thermoregulation. It has been difficult to quantify the prevalence of autonomic dysfunction in PD. First, antiparkinsonian medication with levodopa can decrease blood pressure while standing and delay gastric emptying. Anticholinergics further decrease gastrointestinal motility. Until relatively recently, these abnormalities were believed, incorrectly, to reflect side-effects of the drugs, whereas we now know that the drugs interact importantly with the dysautonomia that is part of the disease process itself. Second, the parkinsonian form of multiple system atrophy (MSA-P), which always features signs and symptoms of autonomic dysfunction, can resemble PD clinically, so that studies can overestimate or underestimate the frequency of autonomic dysfunction by misdiagnosis.

In a retrospective study, almost one-third of patients with pathologically proven PD had autonomic dysfunction documented in the medical record (Rogers et al., 1980). This retrospective approach most likely underestimates the frequency of autonomic failure. Compared to age-matched control subjects, PD patients have higher frequencies of constipation, erectile dysfunction, urinary urgency, incomplete bladder emptying, dysphagia, and orthostatic lightheadedness. Indeed, about 9 in 10 patients with PD have one or more of these autonomic symptoms (Singer et al., 1991). Autonomic problems increase significantly with increasing disease severity (Visser et al., 2004).

Here we review components of the autonomic nervous system and clinical manifestations, diagnosis, and treatment of autonomic abnormalities in PD. We also note similarities and differences between autonomic abnormalities in MSA and PD. MSA is covered elsewhere in this volume (Ch. 19).

Disturbances of Gastrointestinal Motility and the Nervous System

Michael Camilleri, Adil E. Bharucha, in Aminoff's Neurology and General Medicine (Fifth Edition), 2014

Acute Peripheral Neuropathy

Autonomic dysfunction associated with certain acute viral infections may result in nausea, vomiting, abdominal cramps, constipation, or a clinical picture of pseudo-obstruction. In the Guillain–Barré syndrome, visceral involvement may include gastric distention or adynamic ileus. Persistent gastrointestinal motor disturbances may also occur in association with herpes zoster, Epstein–Barr virus infection, or botulism B. The site of the neurologic lesion is uncertain. Cytomegalovirus has been identified in the myenteric plexus in some patients with chronic intestinal pseudo-obstruction. Selective cholinergic dysautonomia (with associated gastrointestinal dysfunction) has been reported to develop within a week of the onset of infectious mononucleosis.[23] Diarrhea induced by human immunodeficiency virus (HIV)

reported to develop within a week of the onset of infectious mononucleosis.[25] Diarrhea induced by human immunodeficiency virus (HIV) may be another manifestation of autonomic dysfunction (see later), but the data require confirmation.

Autonomic Nervous System

Eduardo Benarroch, ... Horacio Kaufmann, in Textbook of Clinical Neurology (Third Edition), 2007

MOTOR/REFLEXES/CEREBELLAR/GAIT

Autonomic dysfunction is a frequent accompaniment of central and peripheral motor syndromes. Muscle weakness in the distribution of a peripheral nerve or root may accompany hyperhidrosis or vasomotor changes resulting from nerve injury. Distal symmetrical motor weakness with loss of the deep tendon reflexes indicates a large-fiber peripheral polyneuropathy that can be seen in patients with peripheral demyelinating diseases such as Guillain-Barré syndrome and in those with certain toxic or drug reactions to agents such as vincristine. Proximal muscle weakness and areflexia occur in patients with prejunctional neuromuscular transmission defects that occur with cholinergic autonomic failure, such as botulism[26] and the Lambert-Eaton myasthenic syndrome.

Spastic paraparesis is frequently found in patients with neurogenic bladder and detrusor-sphincter dyssynergia (e.g., as in multiple sclerosis). Areflexia in the lower extremities, which is associated with loss of the anal and bulbocavernosus reflexes, indicates a lesion of the cauda equina that produces hypotonic bladder, bowel hypomotility, and sphincter incontinence. Extrapyramidal, pyramidal, cerebellar, and autonomic deficits in varying combinations are characteristic of multiple system atrophy (i.e., the Shy-Drager syndrome), a neurodegenerative disorder of unknown etiology. Autonomic failure may also accompany Parkinson's disease, with its associated resting tremor, bradykinesia, rigidity, and postural reflex impairment.

ORTHOSTATIC HYPOTENSION

Horacio Kaufmann, Italo Biaggioni, in Neurology and Clinical Neuroscience, 2007

Treatment of Related Conditions

Autonomic failure can be associated with low-production anemia and inappropriately low serum erythropoietin levels. If other causes of anemia are ruled out, patients can be treated with recombinant erythropoietin (25 to 50 U/kg subcutaneously three times per week). Erythropoietin has been shown to improve upright blood pressure,[36,37] and its use may be warranted for this reason alone, rather than as a treatment for anemia.

Many patients may also have supine hypertension resulting from preexisting essential hypertension or as part of autonomic failure.[38] In occasional patients, significant hypertension may be present even in the seated position. During the day, supine hypertension is best managed by simply avoiding the supine position. At night, it is necessary for many patients to take vasodilators at bedtime, after which they should be advised against getting up during the night without assistance. Hydralazine hydrochloride (25 to 100 mg) and low doses of nitrates as transdermal preparations (e.g., Nitro-Dur, 0.1 mg/hour, applied at bedtime and removed on arising) or short-acting calcium channel blockers (e.g., nifedipine, 10 mg) are often useful. A stepwise approach to the management of supine hypertension in the setting of orthostatic hypotension is included in Table 28-3 and discussed in detail elsewhere.[39]

KEY POINTS

- The autonomic nervous system is crucial for the regulation of blood pressure in general and for maintaining orthostatic hemodynamics in particular. Disorders associated with autonomic impairment are often characterized by disabling orthostatic hypotension.
- Systemic illnesses producing peripheral neuropathy can cause secondary autonomic failure. Primary autonomic failure is caused by neurodegenerative disorders with neuronal or glial deposits of α-synuclein, including Parkinson's disease, dementia with Lewy bodies, pure autonomic failure, and multiple-system atrophy (Shy-Drager syndrome).
- Subacute onset of autonomic failure and rapid progression can be caused by an autoimmune autonomic disorder or may be a paraneoplastic syndrome.
- The hallmark of autonomic failure is profound orthostatic hypotension without an appropriate compensatory increase in heart rate. Autonomic function tests are usually confirmatory, but the differential diagnosis can be challenging.
- There is currently no treatment to cure or delay the progression of disease. Symptomatic treatment of orthostatic hypotension is often successful and relies on a combination of nonpharmacological measures, blood and plasma volume enhancement, and short-acting pressor agents taken before upright activity rather than at fixed intervals.
- About half of the patients with autonomic failure paradoxically develop supine hypertension, which is managed during the day

by simply avoiding the supine posture but may necessitate pharmacological treatment during the night.

Neurologic Diseases

Benjamin K. Scott MD, Dimitry Baranov MD, in Anesthesia and Uncommon Diseases (Sixth Edition), 2012

Neurodegenerative disorders with autonomic failure

Autonomic failure (or dysautonomia), with its protean range of manifestations and symptoms, is a common part of an immensely diverse group of disorders in which some or all elements of the autonomic nervous system are affected. Autonomic failure to varying degrees is a part of the presentation of many systemic diseases (e.g., diabetes mellitus, amyloidosis), infectious diseases (e.g., leprosy, human immunodeficiency virus [HIV], rabies), immune disorders (e.g., acute dysautonomia, Guillain-Barré syndrome), paraneoplastic disorders, hereditary autonomic disorders (e.g., all HSANs, dopamine β-hydroxylase deficiency), and neurodegenerative disorders. A comprehensive discussion on various aspects of autonomic dysfunction in these conditions can be found in most neurology and medical textbooks. This section discusses only the most prevalent neurodegenerative disorders in which autonomic failure plays a prominent role, presenting a significant anesthetic challenge.

Parkinson's disease (PD), dementia with Lewy body disorder (LBD), multiple system atrophy (MSA), and pure autonomic failure disorder (PAF) are all neurodegenerative disorders of unclear etiology, presenting with variable degrees of autonomic dysfunction. Based on the differences in the neuropathology, these disorders can be divided into two subgroups: Lewy body syndromes (PD, LBD, and PAF) and multiple system atrophy. All these disorders are characterized by the presence of α-*synuclein* in the neuronal cytoplasmic inclusions (Lewy bodies, as in Lewy body syndromes) or the glial cell inclusions (GCIs, as in MSA); thus these disorders are often called *synucleinopathies.* In PD, neurodegeneration is predominant in the substantia nigra and other brainstem nuclei and in peripheral autonomic neurons. Motor dysfunction is more prominent than autonomic failure in PD patients. Neuronal degeneration in PAF is restricted to peripheral autonomic neurons; thus the symptoms of pure autonomic failure without other manifestations. Extensive cortical involvement, in addition to degeneration of brainstem nuclei and peripheral autonomic neurons, is characteristic for LBD, which presents as severe dementia associated with parkinsonism and autonomic failure.

In MSA, cytoplasmic inclusions are found in the glial cells (GCIs) and not neurons (Lewy body). These inclusions are associated with degenerative changes in the central neurons in basal ganglia, cortex, and spinal cord, but not in peripheral autonomic neurons. Two phenotypes of MSA are currently identified based on the predominant clinical picture of *parkinsonism* (MSA-P) or *cerebellar dysfunction* (MSA-C). In the past, the patients with a predominant picture of autonomic failure were diagnosed with Shy-Drager syndrome. Currently, this term is rarely used, because all patients with MSA have a significant degree of autonomic dysfunction.[47]

Autonomic failure in patients with Lewy body syndromes and MSA typically manifests with orthostatic and postprandial hypotension, bladder dysfunction, gastrointestinal (GI) motility disorders, and erectile dysfunction (ED). Orthostatic and postprandial hypotension is often the earliest and most disabling aspect of dysautonomia in many patients. Other symptoms of autonomic dysfunction, as described for familial dysautonomia, can be present. The differential diagnosis can be difficult because of frequent overlapping of the clinical picture between these conditions, especially in the initial stages of the disease process. Definitive diagnosis in some disorders could be established only on postmortem histopathologic examination. However, thorough clinical examination helps to distinguish between PD, LBD, MSA, and PAF (Table 8-2). The subject of neurodegenerative disorders with autonomic failure has been reviewed.[47,48]

Anesthetic management of PD is described later. Although LBD is the second most common cause of dementia after Alzheimer's disease, there are no reports of anesthetic management in the literature. It appears reasonable to assume that the principles of anesthetic management of patients with LBD are common to those in patients with other forms of dementia. In LBD patients with advanced dysautonomia, the same precautions should be taken as in patients with MSA.

Multiple System Atrophy

In 1998, consensus committees representing the American Autonomic Society and the American Academy of Neurology defined multiple system atrophy as a sporadic, progressive, neurodegenerative disorder of undetermined etiology, characterized by features in the three clinical domains of parkinsonism, autonomic failure, and cerebellar or pyramidal dysfunction. In the past, the terms striatonigral degeneration, olivopontocerebellar atrophy, and Shy-Drager syndrome were used, depending on the predominance of clinical symptoms in any of these three domains.

Multiple system atrophy is a fatal disease that typically presents in the fourth to sixth decade of life, with mean disease duration of 6 years from onset of symptoms. Because of the significant similarity of clinical presentation to other neurodegenerative disorders, MSA is often not diagnosed until later stages. *Parkinsonism* is a predominant symptom in 80%, and cerebellar dysfunction in 20%, of all patients. Parkinsonism is usually not responsive to antiparkinsonian medications, which helps to differentiate MSA from PD. The most common and early presentation of autonomic dysfunction is urinary incontinence and ED. Orthostatic hypotension is found in half of MSA patients and is usually mild. Reduced heart rate variability and absence of compensatory tachycardia during hypotension is characteristic

and is usually mild. Reduced heart rate variability and absence of compensatory tachycardia during hypotension is characteristic. Paradoxically, supine hypertension is present in more than half of patients and complicates their management. Recurrent syncope is a sign of severe orthostatic hypotension. Severe constipation, fecal incontinence, and decreased sweating are other signs of autonomic dysfunction in MSA.

Obstructive sleep apnea or central sleep apnea and sleep-related inspiratory stridor associated with bilateral vocal cord paresis or dysfunction have been reported in MSA patients.[49]

There are no currently available treatments that can modify the clinical course or address the underlying pathologic MSA process. All the treatments are symptomatic, intended for improving the quality of life in these patients. Orthostatic hypotension is treated with administration of fludrocortisone or milrinone (oral adrenergic vasoconstrictor). The presence of significant supine hypertension limits the use of vasopressors. Erythropoietin has been reported to be useful in the treatment of patients with associated anemia and severe hypotension. Tracheostomy and respiratory support is reserved for the patients with stridor and central sleep apnea.

Anesthetic considerations

Perioperative management of patients with MSA is a formidable challenge because of potential hemodynamic instability and respiratory compromise in the postoperative period (Box 8-4). A few case reports in the literature indicate no adverse effects to most of the common anesthetic agents.[50-60] The management is directed at ensuring hemodynamic stability through invasive hemodynamic monitoring, adequate preoperative hydration, and maintenance of normovolemia with fluid replacement intraoperatively. Preoperative optimization of fludrocortisone therapy is recommended. Some controversy surrounds the potentially unpredictable response to vasopressor amines because of sympathetic hypersensitivity caused by autonomic denervation.[52,61] Therefore, it is recommended to administer vasoactive medications very cautiously in much smaller doses than usual. However, vasopressors have been used without adverse effects for treatment of hypotension intraoperatively, when titrated judiciously.[53,54,60]

Significant intraoperative supine hypertension has been reported, with minimal response to labetalol but profound hypotension after hydralazine administration.[62] The hypotension responded only to vasopressin infusion. Short-acting vasodilators such as sodium nitroprusside may be a better choice for intraoperative supine hypertension. The hypertensive episodes in autonomic failure are particularly responsive to transdermal nitroglycerin.[63]

Neuraxial anesthesia techniques have been successfully employed in patients with MSA, including for labor and delivery, with a greater degree of hemodynamic stability, also avoiding possible difficulties with extubation in these patients.[51,56,57,59,64] It is speculated that patients with autonomic failure are less likely to respond with hypotension to sympathectomy caused by neuraxial block because they are already sympathectomized. The data in the literature support this hypothesis.

When general anesthesia is chosen, careful planning for extubation and postoperative monitoring of the respiration in the ICU setting is warranted, especially in MSA patients with a history of stridor or central or obstructive sleep apnea.

Pure Autonomic Failure

Pure autonomic failure is a sporadic, slow-progressing neurodegenerative disorder of the autonomic nervous system (ANS) that typically affects individuals in the sixth decade of life. PAF is characterized by an isolated impairment of the peripheral and central ANS. No symptoms of parkinsonism, cerebellar dysfunction, or dementia are usually present. The orthostatic hypotension in this syndrome is typically severe and more disabling than in other neurodegenerative disorders with autonomic failure. Other symptoms of autonomic failure are similar to those seen in MSA. The prognosis in PAF patients, however, is much better.

There is only one case report in the literature of general anesthesia without complications in a patient with PAF;[65] it is unclear whether the patient also had epidural anesthesia performed. However, the authors advocate the use of epidural anesthesia and invasive hemodynamic monitoring for greater hemodynamic stability.

The same principles of anesthetic management used for patients with MSA should be applied when managing PAF patients.

Paraneoplastic Autonomic Dysfunction

Ramesh K. Khurana, in Primer on the Autonomic Nervous System (Third Edition), 2012

Autonomic Neuropathy

Autonomic dysfunction may occur with minimal or no somatic involvement. There is subacute onset of orthostatic, gastrointestinal, genitourinary, and pupillary symptoms. Autonomic tests show widespread parasympathetic and sympathetic dysfunctions. The patients may be seropositive for ganglionic acetylcholine receptor (AchR) autoantibodies. Serum ganglionic AchR antibody levels correlate with severity of autonomic dysfunction. Administration of these antibodies to mice results in autonomic dysfunction. Experimental autoimmune autonomic ganglionopathy can be reproduced in rabbits by immunizing against AchR.

Lambert–Eaton Myasthenic Syndrome

Lambert–Eaton myasthenic syndrome (LEMS) presents with symmetrical proximal weakness, reduced or absent reflexes, and ptosis

Lambert–Eaton myasthenic syndrome (LEMS) presents with symmetrical proximal weakness, reduced or absent reflexes, and ptosis. Autonomic symptoms (subclinical excepting dry mouth) occur in about 75% of patients. Autonomic tests show widespread cholinergic and adrenergic abnormalities. The electrophysiological hallmarks are low amplitude of the compound muscle action potentials, decremental responses on 2- to 5-Hz nerve stimulation, and augmentation >100% on 20- to 50-Hz stimulation or following 10 seconds of voluntary exercise. Almost all patients show autoantibody against PQ-type voltage-gated calcium channels (VGCC). Autoantibodies against N-type VGCC, important for transmitter release from autonomic nerve terminals are reported in about 30% of patients. Pathogenecity of the VGCC antibodies is proved by expression of VGCC antigen on cancer cells, passive transfer of the human disorder to mice with the injection of LEMS IgG, antibody binding to the active zone particles (AZPs) of the presynaptic calcium channels, reduced number and disorganization of AZPs demonstrated by freeze-fracture studies of the patient's neuromuscular junction, reduced presynaptic quantal release of acetylcholine, and relatively rapid improvement following removal of antibodies with plasma exchange. LEMS IgG, found to impair transmitter release from parasympathetic (bladder) and sympathetic (vas deferens) neurons, is probably responsible for autonomic dysfunction. However, contribution of other factors such as antibodies against neuronal ganglionic acetylcholine receptor cannot be excluded.

Autoimmune Neurology

Andrew Mckeon, Eduardo E. Benarroch, in Handbook of Clinical Neurology, 2016

Guillain–Barré syndrome

Autonomic dysfunction is common in Guillain–Barré syndrome (GBS), particularly in patients with severe motor deficits, and may manifest with hypo- or hyperactivity (Zochodne, 1994; Low et al., 2003; van Doorn et al., 2008). Autonomic failure may precede the onset of motor weakness and may be a prominent feature in some patients (Koike et al., 2013). Autonomic complications, together with sepsis, are the major cause of death in GBS. During the acute phase of GBS, dysautonomia is dominated by sympathetic hyperactivity, manifested with hypertension, hyperhidrosis, and resting tachycardia. Blood pressure fluctuations, with hypertension alternating with hypotension, may occur as manifestation of baroreflex failure. Parasympathetic failure is more evident during recovery. Gastrointestinal dysmotility is common and may progress to ileus in up to 15% of cases (Burns et al., 2001). Typically, autonomic neuropathy improves in concert with improvement of motor and sensory nerve functions. However, long-term autonomic sequelae are common and may be detectable in autonomic laboratory testing.