



Subject: Autonomic Testing
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Description/Scope

This document addresses the use of autonomic testing. This document does not address the use of tilt-table testing.

Note: Please see the following related document for additional information:

• CG-LAB-13 Skin Nerve Fiber Density Testing

Position Statement

Investigational and Not Medically Necessary:

The use of autonomic nervous system function testing for sudomotor function using quantitative sudomotor axon reflex test (QSART), the thermoregulatory sweat test (TST), silastic sweat imprint, sympathetic skin response (SSR), quantitative direct and indirect reflex test of sudomotor function (QDIRT), or SudoScan are considered **investigational and not medically necessary** for all indications.

The use of autonomic nervous system function testing for cardiovagal innervations is considered investigational and not medically necessary for all indications.

The use of autonomic nervous system function testing for vasomotor adrenergic innervations is considered investigational and not medically necessary for all indications.

Rationale

Sudomotor Testing

Sudomotor testing is used to evaluate the small nerve fibers associated with sweating and aid in the evaluation of neuropathy, specifically assessing distal sympathetic polyneuropathy. A 2021 consensus statement on electrodiagnostic assessment of the autonomic nervous system endorsed by the American Autonomic Society, American Academy of Neurology, and the International Federation of Clinical Neurophysiology (Cheshire, 2021) states:

Autonomic peripheral neuropathies are subject to investigation and quantification by electrodiagnostic autonomic testing. Laboratory evidence of autonomic neuropathy may be found with or without corresponding symptoms. The most common laboratory changes comprise a concomitant involvement of distal postganglionic sudomotor and cardiovagal autonomic neuropathy without orthostatic hypotension.

The guidance is based on expert consensus and included the following recommendations:

Testing of the autonomic nervous system in the clinical autonomic laboratory should be performed by healthcare professionals with comprehensive knowledge of the neuroanatomy, physiology, and pathological profiles of autonomic disorders. Interpretation of autonomic test results should be based also on a medical history and physical examination, from which autonomic testing assists in confirming or eliminating potential conditions in a differential diagnosis.

A combination of autonomic tests in a screening battery provides a more accurate measure of autonomic function, as a single test alone cannot distinguish the type or severity of autonomic failure. Ideally, assessment of autonomic function should include tests of cardiovascular adrenergic, cardiovagal, and sudomotor function. In resource limited settings the knowledge and expertise of the person interpreting autonomic tests is no less important. Before the results are interpreted as normal or abnormal, consideration should be given to potentially confounding factors, such as medications, equipment settings, room conditions, or patient factors that might have altered the findings.

A study by Gibbons et al (2008) describes a new technique to assess sudomotor function using the quantitative direct and indirect reflex test of sudomotor function (QDIRT). Ten participants had stimulated sweat on both forearms. Impressions were made and indicator dyes were photographed every 15 seconds for 7 minutes. The droplets of sweat were measured by size, location and percent surface area. Each participant had the tests again eight more times on alternating arms over a 2-month period. Another 10 participants had impressions, QDIRT, and quantitative sudomotor axon reflex test (QSART) performed on the right foot. The percent of sweat that was photographed correlated with the silicone impressions at 5 minutes on the forearm and foot. The number of sweat droplets measured with QDIRT correlated with the silicone impression. And while QDIRT measured the sudomotor response with temporal resolution that is similar to QSART and spatial resolution that is similar to silicone impressions, there are limitations to QDIRT such as ambient room temperature and lack of humidity control. There is no information provided about the clinical utility of QDIRT and the authors state "Additional investigation is necessary to determine the utility of QDIRT in disease states that alter sudomotor structure or function."

Cardiovagal and Adrenergic Testing

Cardiovagal innervations and vasomotor adrenergic innervations can be used to assess conditions such as tachycardia and orthostatic hypotension. Postural tachycardia syndrome (POTS) is a condition defined as orthostatic intolerance with heart rate increments greater than 30 beats/minute on head-up tilt test. Some of the symptoms can include syncope, palpitations, and lightheadedness. A study by Kimpinski (2012b) reported on 58 individuals with POTS who received autonomic testing and were followed for 1 year. All participants received the following autonomic testing: QSART, heart rate response to deep breathing and Valsalva ratio; blood pressure and heart rate responses to Valsalva maneuver; and head-up tilt. Fifty-four participants were available for the 1-year follow-up. All participants were given information about conservatively treating their orthostatic symptoms at baseline and at the 1-year follow-up. At baseline, 20 participants were taking β-blockers and 28 were taking them at 1 year. The dosages were not significantly different at 1 year when compared to baseline. The heart rate increment during head-up tilt did not significantly differ between baseline and 1 year, but 20 of the participants no longer met the criteria for POTS. With no significant changes in dosages in medications from baseline to 1-year follow-up, it is unclear how autonomic testing influenced clinical management.

A 2012 retrospective review by Sukul looked at 142 children who had autonomic testing consisting of tilt table test, Valsalva maneuver, cardiac response to deep breathing, QSART, and thermoregulatory sweat test (TST) in a minority of children. The relevance of the autonomic test results to clinical presentation was ranked using a 3-point scale with 1 being unhelpful, 2 was somewhat helpful and 3 was very helpful. After review of clinical data, the treatments prescribed following autonomic testing were recorded and any associated symptom benefit was ranked on a 5-point scale with 1 = severe worsening of symptoms, 2 = mild worsening of symptoms, 3 = no change in symptoms, 4 = mild symptom relief, 5 = excellent symptom relief. POTS was the most frequently revealed condition following autonomic testing with orthostatic hypertension being the least frequently revealed. The tests were normal in 4% of the participants, Valsalva maneuver was abnormal in 15%, and deep breathing was abnormal in 13%. Treatment following autonomic testing included β -blockers, vitamin supplements and salt supplements. B-blockers were prescribed in 30/142 of the children. Symptom relief (rank 4 or 5) following treatment was reported in 73% of children. While this study may show autonomic testing influenced treatment plans, the study has several limitations including 1) a retrospective design that permits inferences about associations not causation, 2) many children whose testing was normal did not undergo follow-up in the clinics where the testing was done so their data was unavailable for analysis, 3) the demographics of the study population were partially a product of the referral of the practice, and 4) there was a variable length of follow-up which does not allow for determination whether symptom benefit/detriment may have occurred in some children unrelated to treatment.

Peltier and colleagues (2010) published the results of a study aimed at determining the incidence of sudomotor abnormalities and the relationship between QSART findings and other biochemical and physiological measures of autonomic function in a well characterized inpatient cohort of individuals with POTS. The study involved 30 individuals who were free of medications that could alter autonomic tone for at least 5 half-lives and placed on a controlled diet. A total of 17 (56%) participants had abnormal QSART which was typically patchy and involved the lower extremity, while 13 (43%) participants had normal QSART results. Other autonomic tests such as catecholamines and spectral indices did not correlate with QSART results. No differences in autonomic tests or spectral indices were observed between hyperadrenergic and non-hyperadrenergic POTS. The results indicate that a subset of individuals with POTS have sudomotor abnormalities which are typically patchy in distribution that do not correlate with other tests of autonomic function. Larger controlled studies are needed to determine the optimal methods of endophenotyping individuals with POTS.

Zhang and colleagues (2022) published a retrospective review of the medical records of 356 individuals with POTS. A total of 211 (59%) of the individuals underwent QSART, 80 (22%) underwent skin biopsy, 51 (15%) had both types of testing. The median time between QSART and skin biopsy was 4 weeks. There was poor agreement between the results of QSART and skin biopsy among individuals who had both tests. The study found that 70 (33%) of the individuals who underwent QSART had reduced sweat output in at least one of the four testing sites. In addition, 19 (24%) individuals who underwent skin biopsy had reduced intrapidermal nerve fiber density (IENFD) in at least one site. Compared to individuals with normal IEFND, those with reduced IENFD were significantly older; there were no significant differences in the two groups in terms of comorbid autoimmune disease or frequency of reported symptoms. This study was designed to characterize a cohort of individuals with POTS, not to evaluate the diagnostic accuracy of autonomic testing.

The American College of Cardiology/American Heart Association/Heart Rhythm Society guideline for the evaluation and management of syncope (Shen, 2017) states referral for autonomic evaluation "can be useful to improve diagnostic and prognostic accuracy in selected patients with syncope and known or suspected neurodegenerative disease."

Neurodegenerative Diseases

Multiple system atrophy (MSA) is a progressive neurodegenerative disorder which is characterized by symptoms of autonomic nervous system failure such as fainting spells, orthostatic hypotension, bladder control problems and motor control symptoms. There is no cure for MSA and treatment is aimed at controlling symptoms. Diagnosis is made using clinical criteria initially established by a consensus conference in 1998 and reviewed and modified by a second consensus conference in 2007 (Gilman, 2008). While autonomic dysfunction is required to establish the diagnosis of definite, probable, or possible MSA or MSA with predominant Parkinson or predominant cerebellar ataxia, the specific testing described in this document is not essential for the diagnosis of MSA.

Lipp (2009) prospectively evaluated the autonomic systems differences between 52 MSA subjects and 29 Parkinson subjects noting that the autonomic deficits present at the onset of the study continued and increased during the 1-year follow-up period.

A retrospective review by lodice (2012) sought to evaluate if premorbid autonomic testing and consensus criteria are accurate in autopsy confirmed MSA. Twenty-nine individuals were identified; all 29 received autonomic testing and subsequently had MSA confirmed with autopsy findings. All of the individuals had QSART; 8 had normal results, 10 had reduced widespread postganglionic sudomotor function. The remaining participants had either patchy, distal or length dependent, or focal postganglionic sudomotor function. Twenty-two individuals had TST, 2 of which had normal results, the other 20 individuals had anhidrosis with 18 having anhidrosis greater than 30%. Composite Autonomic Severity Score (CASS) was 7.2 ± 2.3 and defined as severe. The authors concluded the presence of severe generalized autonomic failure, widespread anhidrosis, and rapid progression of autonomic failure is highly predictive of multiple system atrophy.

Researchers have explored whether autonomic testing enhances the clinical differentiation between MSA and Parkinson disease. Kimpinski (2012a) looked at 29 subjects including 10 subjects with Parkinson disease, 9 subjects with MSA and 10 healthy controls matched for age and gender. Findings indicated differences in the presentation of autonomic dysfunction in MSA vs. Parkinson disease. Specifically, that autonomic dysfunction is generalized and predominantly preganglionic in multiple system atrophy, and postganglionic in Parkinson's disease. The authors conclude by acknowledging their small study sample and stating that, "further confirmatory studies using larger patient numbers are required."

In 2020, Indelicato and colleagues sought to evaluate the diagnostic yield of cardiovascular autonomic function tests as an aid in the root-cause investigation of cerebellar ataxia. A series of cardiovascular autonomic tests were administered to a cohort of individuals with neurodegenerative cerebellar ataxia, as well as matched healthy controls. Sporadic cases were followed-up (median 15 months [range 12-33 months]) for an eventual conversion to MSA-C (cerebellar type). A total of 42 individuals with cerebellar ataxia were recruited (n= 23 hereditary cases and n=19 sporadic cases [2 probable MSA-C, 6 possible MSA-C, 11 sporadic adult-onset ataxia]). Sporadic and hereditary cases showed no difference concerning ataxia severity at baseline. At head-up tilt, non-orthostatic hypertension blood pressure-related falls were detected in 9 cases (n=7 sporadic cases and n=2 hereditary cases), but 0 matched controls. A total of 5 of 7 sporadic cases with a non-orthostatic hypertension blood pressure-related fall post head-up tilt test, converted to possible or probable MSA-C. Authors concluded, in the work-up of cerebellar ataxia, a battery of cardiovascular autonomic tests may detect early signs of blood pressure dysregulation, potentially alluding to an underlying or developing possible/probablable MSC-C etiology. Studies determining the clinical utility of these cardiovascular autonomic tests and their impact on net health outcomes are warranted.

Sudoscan technology has been studied in the evaluation of identifying autonomic neuropathy in people with Parkinson's disease. In a 2019 study by Xu and colleagues, the authors assessed sudomotor function in individuals with Parkinson's disease using Sudoscan. They analyzed risk factors for autonomic neuropathy using electrochemical skin conductance, which can be recorded with Sudoscan. Included in the study were 43 individuals in the later stages of Parkinson's disease and 42 individuals serving as controls. The authors noted electrochemical skin conductance of the hands and feet was reduced lower in the Sudoscan group compared to the control

group; 28% lower in the hands and 19.1% lower in the feet of the individuals with Parkinson's disease. Conversely, in a 2019 study by Popescu and colleagues, 67 individuals with moderate stage idiopathic Parkinson's disease had evaluation of small fibers function by electrochemical skin conductance using Sudoscan technology compared to 66 age-matched controls. The authors noted no significant reduction in electrochemical skin conductance in the individuals with Parkinson's disease versus the control group. Popescu does note the Xu 2019 study was conducted on individuals with later stages of Parkinson's disease compared to moderate stages in their cohort. Larger studies are necessary to evaluate efficacy.

Diabetes

Numerous studies have explored the presence and impact of autonomic dysfunction in individuals with diabetes. A 2004 study by Low and colleagues looked at 231 participants with diabetes and 245 healthy age-matched controls and aimed to estimate comprehensive autonomic symptom profile in diabetes using a laboratory evaluation of autonomic function and a validated self-report. Autonomic neuropathy was found to be present in 54% of type 1 diabetics and 73% of type 2 diabetics.

A retrospective review by Chen and colleagues (2008) looked at 674 individuals with type 2 diabetes who complained of autonomic-like symptoms or who presented with clinical manifestations of diabetic autonomic neuropathy. These individuals underwent heart rate variation testing and postural blood pressure testing. Participants had also completed a questionnaire in which they were asked about autonomic-like symptoms experienced during the previous year. Of the 674 individuals in the analysis, 562 of them complained of at least one autonomic symptom. For the asymptomatic individuals, 47% of them showed to have autonomic neuropathy upon testing. The authors also noted that the more autonomic symptoms an individual complained about, the higher their prevalence of autonomic neuropathy.

A 2008 study by Lykke and colleagues followed 391 type 1 diabetic individuals for 10 years to investigate the effect of cardiovascular autonomic neuropathy on morbidity and mortality. During the follow-up period, 62 individuals died (43 of them were due to cardiovascular events). Individuals with borderline heart rate variation did not have mortality rates significantly different from those individuals with normal heart rate variation. For those individuals who had decreased heart rate variability, there was an excess overall mortality that diminished after adjusting for conventional cardiovascular risk factors compared to individuals with normal heart rate variability.

Maguire (2007) retrospectively studied the significance of subclinical autonomic nerve test abnormalities in adolescents. A total of 59% of the original study group who had undergone autonomic testing were available for a 12-year follow up. There was no association between cardiovascular testing and complications related to diabetes, however the authors suggest an association between baseline pupillometry tests and the presence of microalbuminuria and retinopathy at 12 years of follow-up. This study is methodologically limited in part by a retrospective design and the limited number of children available for follow up. The clinical utility of this finding is uncertain.

A study by Eranki and colleagues (2013) reported on the use of Sudoscan as a screening tool for microvascular complications in type 2 diabetes. A total of 309 participants with type 2 diabetes were included in the study. At least one microvascular complication was found in 120 participants (79% had peripheral neuropathy, 43% had retinopathy, and 23% had nephropathy). At least two microvascular complications were found in 46 participants. Nine participants had all three microvascular complications. The sensitivity of the risk score using 35% as the cut-off for detection of least one microvascular complication was 82% and the specificity was 61%. For detection of peripheral neuropathy, sensitivity was 82% and specificity was 55%. Detection of retinopathy showed a sensitivity of 74% and specificity was 63% while detection of nephropathy showed sensitivity of 76% and specificity of 68%. This study has limitations which include the fact that it was performed in a limited population, peripheral neuropathy was based only on biothesiometer results, nephropathy was based only on Modification of Diet in Renal Disease and retinopathy was based on fundoscopy. It was also a cross-sectional study which should have a follow-up study.

Krieger and colleagues (2018) reported on a study of participants who received Sudoscan technology (using skin electrochemical conductance) for diagnosing diabetic polyneuropathy which was compared to QSART. A total of 47 participants with type 2 diabetes (20 without diabetic polyneuropathy, 27 with diabetic polyneuropathy) and 16 matched controls were examined for neuropathic symptoms and for the extent of sensory deficits. A modified version of the clinical scoring systems Neuropathy Disability Score and Neuropathy Symptoms Score was used to evaluate neuropathic symptoms and the severity of sensory deficits. Nerve conduction studies were used to evaluate nerve function and to determine the presence of diabetic peripheral neuropathy. The skin electrochemical conductance average of the feet was smaller in participants with diabetic peripheral neuropathy than the control group. The skin electrochemical conductance average of the hands was lower in participants with diabetic peripheral neuropathy as compared to those without neuropathy and the control group. Skin electrochemical conductance showed a sensitivity and specificity of feet and hands for detecting diabetic peripheral neuropathy of 70/85% and 53/50% respectively while QSART could not differentiate between the three groups. The lower skin electrochemical conductance of feet and hands was correlated with a higher Neuropathy Disability and Neuropathy Symptoms scores. While this study suggests that Sudoscan technology can be used as a screening tool for diabetic peripheral neuropathy, it is unclear how results of this technology can affect clinical management, treatment or notable health outcomes of the disease.

Syngle and colleagues (2021) reported on a prospective, open-label study assessing the efficacy and tolerability of teneligliptin on autonomic and peripheral neuropathy in 20 individuals with type 2 diabetes. Efficacy parameters included Sudoscan score; parasympathetic dysfunction assessment using Ewing's criteria (heart rate response to standing, Valsalva, and deep breath); sympathetic dysfunction assessed as blood pressure response to standing and handgrip; ankle brachial index; vibration perception threshold (VPT); C-reactive protein; and glycemic profile. After 12 weeks of treatment, there was improvement in heart rate response to standing and Valsalva (p<0.01), but not to deep breath (p=0.12). Blood pressure response to standing was significantly lowered (p<0.01), but not in response to handgrip (p=0.06). Sudoscan score was increased while VPT was significantly decreased (p<0.01). The authors indicate that the increase in Sudoscan score observed with the decrease in VPT uncovers the coexistence of sudomotor dysfunction and peripheral neuropathy in individuals with diabetes and the significant change in scores of the Ewing's batteries of tests evident the association of autonomic dysfunction with sudomotor dysfunction. Limitations of the study include its size, limited statistical power, lack of placebo control, and lack of confirmation for the diagnosis of peripheral neuropathy using nerve conduction velocity or electromyography studies.

Zhao and colleagues (2022) compared findings of Sudoscan and electromyography (EMG) findings in 326 hospitalized individuals with type-1 or type-2 diabetes. All participants underwent a Sudoscan sweat function test and an EMG examination during hospitalization. A total of 176 of the 326 individuals (54%) had abnormal Sudoscan results and 299 (92%) had abnormal EMG results. Consistency between Sudoscan and EMG results was 53%; the consistency of findings was not statistically significant (p=0.868). The sensitivity and specificity of the Sudoscan for diagnosing distal symmetric polyneuropathy (DSPN) were 53.5% and 48.2%, respectively.

Much of the literature on the Sudoscan in diabetes is limited to small group sizes (Calvet, 2013; Casellini, 2013; Keet, 2014; Smith, 2014). While a study by Yajnik and colleagues (2012) compared Sudoscan to conventional measures of peripheral and cardiac neuropathy in 265 individuals with type-2 diabetes, the authors of that study noted that the Sudoscan is not a substitute for conventional neuropathy testing.

The Heart Rhythm Society (Sheldon, 2015) published an expert consensus statement on the diagnosis and treatment of POTS, inappropriate sinus tachycardia, and vasovagal syncope. The following recommendation was made on the investigation of POTS:

 Detailed autonomic testing, transthoracic echocardiogram, tilt-table testing, and exercise stress testing may be considered for selected patients being assessed for POTS. (Class IIb; Level E)

The same expert consensus statement included the following recommendation on the investigation of inappropriate sinus tachycardia:

It might be worth considering autonomic testing. (Class IIb; Level E)
 Recommendation Class IIb: benefit equivalent or possibly exceeding risk.
 Recommendation Level E: consensus opinion in the absence of credible published evidence.

The American Diabetes Association (2022) recommendations on neuropathy screening and treatment state:

- All patients should be assessed for diabetic peripheral neuropathy starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter. (B)
- Assessment for distal symmetric polyneuropathy should include a careful history and assessment of either temperature or
 pinprick sensation (small fiber function) and vibration sensation using a 128-Hz tuning fork (for large fiber function). All patients
 should have annual 10-g monofilament testing to identify feet at risk for ulceration and amputation. (B)
- Symptoms and signs of autonomic neuropathy should be assessed in patients with microvascular complications. (E)
 Recommendation ratings B: supportive evidence from well conducted cohort studies.
 Recommendation ratings E: expert consensus or clinical experience.

In summary, while some autonomic tests may be used as part of a diagnostic evaluation for select disorders associated with a dysfunction of the autonomic nervous system, there is a paucity of evidence documenting how autonomic tests change disease management or impact treatment and health outcomes in clinical disorders associated with autonomic nervous system dysfunction.

Background/Overview

The autonomic nervous system controls many of the involuntary actions such as blood pressure, heart rate, thermoregulation, respiration, gastrointestinal emptying, bladder function and sexual function. Dysfunction of the autonomic nervous system can present as a primary disorder or be the secondary result of other diseases such as Parkinson's disease or diabetes or related to drugs or alcohol abuse. The entire autonomic nervous system can be affected by disease or disease can be more regionally limited. Treatment is directed toward the underlying disease, if known, but can also be limited to symptom improvement.

Quantitative, non-invasive and reproducible tests are available to assist clinicians in testing autonomic function. Autonomic nervous system testing can be grouped into three categories: sudomotor, cardiovagal innervation, and vasomotor adrenergic innervation. The tests for sudomotor function can include QSART, TST, SSR, Silastic sweat imprint, Sudoscan and QDIRT. The Sudoscan is a non-invasive method to measure sweat gland function. The device evaluates sweat gland function by obtaining electrochemical reaction between sweat chlorides and stainless-steel electrodes. The tests for cardiovagal response can include heart rate response to deep breathing and Valsalva ratio. The tests for adrenergic function include the beat-to-beat blood pressure response to tilt table testing, Valsalva maneuver and standing.

Definitions

Autonomic Nervous System: The part of the nervous system which controls involuntary actions.

Quantitative Direct and Indirect Reflex Test: A technique which combines the technique of QSART measuring sudomotor function with temporal resolution and measures spatial resolution (droplet size and number) similar to the sweat imprint technique.

Quantitative Sudomotor Axon Reflex Test: A test to evaluate the integrity of the postganglionic sudomotor system along the axon reflex to define the distribution of sweat loss. This is accomplished by the release of acetylcholine into the skin which activates receptors on the eccrine sweat gland. The sweat response is recorded from four sites (forearm and 3 lower extremity sites) and assessed for deficits.

Sudomotor: Relating to the nerves that stimulate the sweat glands to activity.

Sweat imprint: Formed by the secretion of active sweat glands into a plastic imprint. The test is used to determine the density of sweat glands, sweat droplet size and sweat volume per area.

Sympathetic Skin Response: A change of the electrical potential of the skin. The recorded skin potential comes from the activated eccrine sweat gland. The amplitude and configuration are adjusted by sweat gland epithelium and the overlying epidermis.

Thermoregulatory Sweat Test: A test where sweating is brought on by thermoregulatory warming which results in a rise of core temperature. When the rise in core temperature goes beyond the thermoregulatory set point of the hypothalamus, sweating occurs. TST can check the thermoregulatory sympathetic pathways from the hypothalamus to the eccrine sweat gland by use of an indicator powder mixture. When the body is warmed to a core temperature of 38°C, sweat is recognized by a change in color in the indicator powder. Digital photography is used to document the sweat distribution which can be characteristic of neuropathy, ganglionopathy or generalized autonomic failure.

Valsalva Maneuver: Holding the nostrils closed while blowing air through the nose.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:

CPT

95921

Testing of autonomic nervous system function; cardiovagal innervations (parasympathetic function), including 2 or more of the following: heart rate response to deep breathing with recorded R-R interval, Valsalva ratio, and 30:15 ratio

95922	Testing of autonomic nervous system function; vasomotor adrenergic innervations (sympathetic adrenergic function), including beat-to-beat blood pressure and R-R interval changes during Valsalva maneuver and at least 5 minutes of passive tilt
95923	Testing of autonomic nervous system function; sudomotor, including 1 or more of the following: quantitative sudomotor axon reflex test (QSART), silastic sweat imprint, thermoregulatory sweat test, and changes in sympathetic skin potential
95924	Testing of autonomic nervous system function; combined parasympathetic and sympathetic adrenergic function testing with at least 5 minutes of passive tilt
95999	Unlisted neurological or neuromuscular diagnostic procedure [when specified as Sudoscan testing]

References

Peer Reviewed Publications:

ICD-10 Diagnosis

All diagnoses

- 1. Calvet JH, Dupin J, Winiecki H, Schwarz PE. Assessment of small fiber neuropathy through a quick, simple and non invasive method in a German diabetes outpatient clinic. Exp Clin Endocrinol Diabetes. 2013; 121(2):80-83.
- 2. Casellini CM, Parson HK, Richardson MS, et al. Sudoscan, a noninvasive tool for detecting diabetic small fiber neuropathy and autonomic dysfunction. Diabetes Technol Ther. 2013; 15(11):948-953.
- 3. Chen HT, Lin HD, Won JG, et al. Cardiovascular autonomic neuropathy, autonomic symptoms and diabetic complications in 674 type 2 diabetes. Diabetes Res.Clin.Pract. 2008; 82(2):282-290.
- 4. Eranki VG, Santosh R, Rajitha K, et al. Sudomotor function assessment as a screening tool for microvascular complications in type 2 diabetes. Diabetes Res Clin Pract. 2013; 101(3):e11-13.
- 5. Gibbons CH, Freeman R. Treatment-induced diabetic neuropathy: a reversible painful autonomic neuropathy. Ann Neurol. 2010; 67(4):534-541.
- 6. Gibbons CH, Illigens BM, Centi J, Freeman R. QDIRT: quantitative direct and indirect test of sudomotor function. Neurology. 2008; 70(24):2299-2304.
- Gilman S, Wenning GK, Low PA, et al. Second consensus statement on the diagnosis of multiple system atrophy. Neurology. 2008; 71(9):670–676.
- 8. Gin H, Baudoin R, Raffaitin CH, et al. Non-invasive and quantitative assessment of sudomotor function for peripheral diabetic neuropathy evaluation. Diabetes Metab. 2011; 37(6):527-532.
- 9. Indelicato E, Fanciulli A, Nachbauer W, et al. Cardiovascular autonomic testing in the work-up of cerebellar ataxia: insight from an observational single center study. J Neurol. 2020; 267(4):1097-1102.
- Iodice V, Lipp A, Ahlskog JE, et al. Autopsy confirmed multiple system atrophy cases: Mayo experience and role of autonomic function tests. J Neurol Neurosurg Psychiatry. 2012; 83(4):453-459.
- Keet SW, Bulte CS, Sivanathan A, et al. Cardiovascular autonomic function testing under non-standardised and standardised conditions in cardiovascular patients with type-2 diabetes mellitus. Anaesthesia. 2014; 69(5):476-483.
- 12. Kimpinski K, Iodice V, Burton DD, et al. The role of autonomic testing in the differentiation of Parkinson's disease from multiple system atrophy. J Neurol Sci. 2012a; 317(1-2):92-96.
- 13. Kimpinski K, Figueroa JJ, Singer W, et al. A prospective, 1-year follow-up study of postural tachycardia syndrome. Mayo Clin Proc. 2012b; 87(8):746-752.
- 14. Krieger SM, Reimann M, Haase R, et al. Sudomotor testing of diabetes polyneuropathy. Front Neurol. 2018; 9:803.
- 15. Lipp A, Sandroni P, Ahlskog JE, et al. Prospective differentiation of multiple system atrophy from Parkinson disease, with and without autonomic failure. Arch.Neurol. 2009; 66(6):742-750.
- Low PA, Benrud-Larson LM, Sletten DM, et al. Autonomic symptoms and diabetic neuropathy: a population-based study. Diabetes Care. 2004; 27(12):2942-2947.
- 17. Low PA, Tomalia VA, Park KJ. Autonomic function tests: some clinical applications. J Clin Neurol. 2013; 9(1):1-8.
- 18. Lykke JA, Tarnow L, Parving HH, Hilsted J. A combined abnormality in heart rate variation and QT corrected interval is a strong predictor of cardiovascular death in type 1 diabetes. Scand J Clin Lab Invest. 2008; 68(7):654–659.
- 19. Maguire AM, Craig ME, Craighead A, et al. Autonomic nerve testing predicts the development of complications: a 12-year follow-up study. Diabetes Care. 2007; 30(1):77-82.
- 20. Peltier AC, Garland E, Raj SR, et al. Distal sudomotor findings in postural tachycardia syndrome. Clin Auton Res. 2010; 20(2):93-99.
- 21. Popescu C. Small fiber neuropathy in Parkinson's disease explored by the sudoscan. Parkinsonism Relat Disord. 2019; 66:261-263.
- 22. Riley DE, Chelimsky, TC. Autonomic nervous system testing may not distinguish multiple system atrophy from Parkinson's disease. J Neurol Neurosurg Psychiatry. 2003; 74(1):56-60.
- 23. Smith AG, Lessard M, Reyna S, et al. The diagnostic utility of Sudoscan for distal symmetric peripheral neuropathy. J Diabetes Complications. 2014; 28(4):511-516.
- 24. Sukul D, Chelimsky TC, Chelimsky G. Pediatric autonomic testing: retrospective review of a large series. Clin Pediatr (Phila). 2012; 51(1):17-22.
- 25. Syngle A, Chahal S, Vohra K. Efficacy and tolerability of DPP4 inhibitor, teneligliptin, on autonomic and peripheral neuropathy in type 2 diabetes: an open label, pilot study. Neurol Sci. 2021; 42(4):1429-1436.
- 26. Xu X, Liao J, Dong Q, et al. Clinical utility of SUDOSCAN in predicting autonomic neuropathy in patients with Parkinson's disease. Parkinsonism Relat Disord. 2019; 64:60-65.
- 27. Yajnik CS, Kantikar VV, Pande AJ, Deslypere JP. Quick and simple evaluation of sudomotor function for screening of diabetic neuropathy. ISRN Endocrinol. 2012; 2012:103714.
- 28. Zhang R, Mayuga K, Shields R, Cantrell C, Wilson R. Skin biopsy and quantitative sudomotor axon reflex testing in patients with postural orthostatic tachycardia syndrome. Cureus. 2022; 14(11):e31021.
- 29. Zhao Y, Bao JJ, Ye LF, Zhou L. Consistency analysis between SUDOSCAN examinations and electromyography results in patients with diabetes. Diabetes Metab Syndr Obes. 2022; 15:3397-3402.

Government Agency, Medical Society, and Other Authoritative Publications:

- American Association of Neuromuscular and Electrodiagnostic Medicine. Proper performance of autonomic function testing. Muscle Nerve. 2017 (reaffirmed 2021); 55(1):3-4.
- American Diabetes Association. Standards of medical care in diabetes--2023. Available at: https://diabetesjournals.org/care/issue/46/Supplement_1. Accessed on January 8, 2024.

- 3. Cheshire WP, Freeman R, Gibbons CH, et al. Electrodiagnostic assessment of the autonomic nervous system: A consensus statement endorsed by the American Autonomic Society, American Academy of Neurology, and the International Federation of Clinical Neurophysiology. Clin Neurophysiol. 2021; 132(2):666-682.
- Sheldon RS, Grubb BP 2nd, Olshansky B, et al. 2015 Heart Rhythm Society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. Heart Rhythm. 2015; 12(6):e41-e63.
- Shen WK, Sheldon RS, Benditt DG, et al. ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2017; 136(5):e60-e122.
- Vinik AI, Camacho PM, Davidson JA, et al. American Association of Clinical Endocrinologists and American College of Endocrinology position statement on testing for autonomic and somatic nerve dysfunction. Endocr Pract. 2017; 23(12):1472-1478

Index

Autonomic Testing

Document History

Status	Date	Action
Reviewed	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated
		Rationale and References sections.
Reviewed	02/16/2023	MPTAC review. Updated Rationale, Background/Overview and References
		sections.
Reviewed	02/17/2022	MPTAC review. Updated Rationale, Definitions, and References sections.
	12/29/2021	Updated Coding section with 01/01/2022 CPT changes; removed 95943 deleted
		12/31/2021.
Reviewed	02/11/2021	MPTAC review. Updated Rationale and References sections.
Reviewed	02/20/2020	MPTAC review. Updated Rationale and References sections.
Reviewed	03/21/2019	MPTAC review. Updated Rationale and References sections.
Reviewed	05/03/2018	MPTAC review. The document header wording updated from "Current Effective
		Date" to "Publish Date." Updated Description/Scope, Rationale, and References
		sections.
Reviewed	08/03/2017	MPTAC review. Updated Rationale and References sections.
Reviewed	08/04/2016	MPTAC review. Updated Rationale and Reference sections. Removed ICD-9 codes
		from Coding section.
Reviewed	08/06/2015	MPTAC review. Updated Rationale.
Revised	08/14/2014	MPTAC review. Added sudoscan testing to the scope of the document. Updated
		Description/Scope, Rationale, Coding and References sections.
Reviewed	08/08/2013	MPTAC review. Updated Description/Scope, Background/Overview, Rationale and
		References.
New	05/09/2013	MPTAC review. Initial document development.
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