Subject: Autonomic Testing
Policy #: MED.00112
Status: Revised
Current Effective Date: 10/14/2014
Last Review Date: 08/14/2014

**Description/Scope**

This document addresses the use of autonomic testing. The autonomic nervous system controls and regulates the internal organs without any conscious recognition or effort. The autonomic nervous system comprises two antagonistic sets of nerves, the sympathetic and parasympathetic nervous systems. When stimulated, the sympathetic nerves prepare the organism for stress by increasing the heart rate, increasing blood flow to the muscles, and decreasing blood flow to the skin. The nerve fibers of the parasympathetic nervous system are primarily the cranial nerves, the vagus nerve, and the sacral spinal nerves. When stimulated, the parasympathetic nerves increase digestive secretions and reduce the heartbeat.

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

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

- [LAB.00020 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**

**General Information**

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 systems 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. Some diagnoses of autonomic disease can be done during a physical exam and work-up to confirm suspected primary disease and may include tests of sudomotor, cardiovagal, and adrenergic function.

**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 2009 Practice Parameter: Evaluation of distal symmetric polyneuropathy: Role of autonomic testing, nerve biopsy and skin biopsy by the American Academy of Neurology (England, 2009) concluded that "Autonomic testing is probably useful in documenting autonomic nervous system involvement in polyneuropathy," with a Classification of Recommendations Level B, meaning "Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population." The authors also point out that the sensitivity and specificity varies among the tests and "Research is necessary to determine whether the documentation of autonomic abnormalities is important in modifying the evaluation and treatment of polyneuropathy."

A study by Gibbons et al (2008) describes a new technique to assess sudomotor function using the 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 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."

**Sudoscan**

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. 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.

**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 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 postural tachycardia syndrome 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 postural tachycardia syndrome. With no significant changes in dosages in medications from baseline to one-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 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. Postural tachycardia syndrome 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%, deep breathing was abnormal in 13%. Treatment following autonomic testing included β-blockers, vitamin supplements and salt supplements. β-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.

The American Heart Association/American College of Cardiology Foundation statement on the evaluation of Syncope (Strickberger, 2006) includes autonomic testing to "confirm the presence of a dysautonomia, distinguish central from peripheral causes, and guide patient management includes tilt table testing, cardiac responses to deep breathing and the Valsalva maneuver, and sweat testing."

**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, probably or possible MSA or MSA with predominant Parkinson or predominant cerebellar ataxia, the specific testing described in this document are not essential for the diagnosis of MSA.

A retrospective review by Iodice (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.
Reseurchers continue to explore whether autonomic testing enhances the clinical differentiation between MSA and Parkinson disease. Kimipinski (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.”

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.

The 2006 American Academy of Neurology Practice Parameter on diagnosis and prognosis of new onset Parkinson disease (PD) analysis of the evidence on which clinical features and diagnostic modalities distinguish PD from other parkinsonian syndromes reports that “Testing of autonomic function may not be useful to distinguish PD from other forms of parkinsonism” and “There is insufficient evidence to support or refute the following as a means of distinguishing PD from other parkinsonian syndromes: urodynamics, autonomic testing, urethral or anal EMG, MRI, brain parenchyma sonography, and FDG PET” (Suchowersky, 2006). While autonomic testing may categorize differences between MSA and Parkinson disease, autonomic testing does not appear to be essential in the diagnosis or management of either MSA or Parkinson disease.

**Diabetes**

Numerous studies have explored the presence and impact of autonomic dysfunction in individuals with diabetes. A 2004 study by Low et al looked at 231 participants with diabetes and 245 healthy age-matched control subjects 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. Fifty-nine (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 uncertain.
Keet and colleagues (2014) reported on a study of 30 individuals with type-2 diabetes who were recruited to complete autonomic function tests under standardized and non-standardized test conditions. The goal was to investigate the reproducibility of autonomic function testing under non-standardized test conditions and standardized test conditions. The level of agreement between heart and pulse rate variability were then compared. The parasympathetic cardiovascular reflex tests included heart rate response during deep breathing, the Valsalva maneuver, and quick standing while the sympathetic tests included blood pressure response during sustained handgrip test and quick standing. Standard test conditions included fasting after midnight and abstinence from smoking and caffeinated beverages. A total of 26 individuals completed non-standardized cardiovascular autonomic function tests under random test conditions. The standardized test conditions were then completed by a subgroup of 14 individuals. The deep breathing test and Valsalva maneuver test were highly reproducible between non-standardized and standardized test conditions. The sustained handgrip and blood pressure response to quick standing results showed a low reproducibility when non-standardized test conditions were compared to standardized test conditions. The study is limited by a small sample size and the authors stated "more evidential value could be obtained with an expanded group of subjects" and "further research is needed to determine whether the derived information can be used to influence pre-operative outcome."

The American Diabetes Association (2014) recommendations on neuropathy screening and treatment state:

- All patients should be screened for distal symmetric polyneuropathy (DPN) starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter using simple clinical tests. (B)
- Electrophysiological testing or referral to a neurologist is rarely needed, except in situations where the clinical features are atypical. (E)
- Screening for signs and symptoms of cardiovascular autonomic neuropathy should be instituted at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes. Special testing is rarely needed and may not affect management or outcomes. (E)
- Medications for the relief of specific symptoms related to painful DPN and autonomic neuropathy are recommended because they may reduce pain (B) and improve quality of life. (E)

Recommendation ratings B: supportive evidence from well conducted cohort studies.
Recommendation ratings E: expert consensus or clinical experience.

*Sudoscan*

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. 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 at 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.

Much of the literature is limited to small group sizes (Calvet, 2013; Casellini, 2013; 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.

There is a paucity of evidence documenting how autonomic tests change management or impact treatment in clinical disorders associated with autonomic nervous systems dysfunction.

**Background/Overview**

The autonomic nervous system regulates blood pressure, heart rate, temperature, respiration, gastrointestinal, bladder and sexual function. 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 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**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>95921</td>
<td>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</td>
</tr>
<tr>
<td>95922</td>
<td>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</td>
</tr>
<tr>
<td>95923</td>
<td>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</td>
</tr>
<tr>
<td>95924</td>
<td>Testing of autonomic nervous system function; combined parasympathetic and sympathetic adrenergic function testing with at least 5 minutes of passive tilt</td>
</tr>
<tr>
<td>95943</td>
<td>Simultaneous, independent, quantitative measures of both parasympathetic function and sympathetic function, based on time-frequency analysis of heart rate variability concurrent with time-frequency analysis of continuous respiratory activity, with mean heart rate and blood pressure measures, during rest, paced (deep) breathing, Valsalva maneuvers, and head-up postural change</td>
</tr>
<tr>
<td>95999</td>
<td>Unlisted neurological or neuromuscular diagnostic procedure [when specified as Sudoscan testing]</td>
</tr>
</tbody>
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**ICD-9 Diagnosis**

[For dates of service prior to 10/01/2015]

All diagnoses

**ICD-10 Diagnosis**

[For dates of service on or after 10/01/2015]

All diagnoses

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**References**

10. Keet SW, Bulte CS, Sivanathan A, et al. Cardiovascular autonomic function testing under non-standardised and...

Government Agency, Medical Society, and Other Authoritative Publications:

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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