Clinical Policy Title: Autonomic nervous system testing and monitoring for neuropathy

Clinical Policy Number: CCP.1005

Effective Date: September 1, 2013
Initial Review Date: February 18, 2013
Most Recent Review Date: April 2, 2019
Next Review Date: April 2020

Policy contains:
- Autonomic nervous system.
- Diabetes.
- Neuropathy.

Related policies:
CCP.1249 Tilt table testing

ABOUT THIS POLICY: Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state and federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

Coverage policy

Select Health of South Carolina considers the use of autonomic nervous system testing and monitoring for neuropathy to be clinically proven and, therefore, medically necessary when overseen and interpreted by a physician of the appropriate specialty (neurologist or cardiologist); to evaluate symptoms of vasomotor instability (e.g., hypotension, orthostatic tachycardia, and hyperhidrosis) after more common causes have been excluded; and for the purpose of achieving a more definitive diagnosis to improve medical decision making to meet any of the following goals:

- To diagnose the presence of autonomic neuropathy in a patient with signs or symptoms suggesting a progressive autonomic neuropathy.
- To evaluate the severity and distribution of a diagnosed progressive autonomic neuropathy.
- To differentiate the diagnosis between certain complicated variants of syncope from other causes of loss of consciousness.
To evaluate inadequate response to beta blockade in vasodepressor syncope.
To evaluate distressing symptoms in a patient with a clinical picture suspicious for distal small fiber neuropathy in order to diagnose the condition.
To differentiate the cause of postural tachycardia syndrome.
To evaluate a change in type, distribution, or severity of autonomic deficits in patients with autonomic failure.
To evaluate the response to treatment in patients with autonomic failure who demonstrate a change in clinical exam.
To diagnose axonal neuropathy or suspected autonomic neuropathy in the symptomatic patient.
To evaluate and treat patients with recurrent unexplained syncope to demonstrate autonomic failure, after more common causes have been excluded by other standard testing (Centers for Medicare & Medicaid Services, 2017).

Limitations:

All other uses of autonomic nervous system monitoring for neuropathy are not medically necessary.

Alternative covered services:

- Physician office visits.
- Appropriate therapy sessions.

Background

The autonomic nervous system, which consists of the sympathetic and parasympathetic systems, regulates physiologic processes without conscious control. Processes affected by the autonomic nervous system include blood pressure, heart rate, body temperature, digestion, metabolism, fluid and electrolyte balance, sweating, urination, defecation, sexual response, and other processes.

Disorders of the autonomic nervous system, including neuropathy, can be primary or secondary to other disorders. Symptoms indicative of autonomic nervous system disorders are multiple; such symptoms can include orthostatic hypotension, heat intolerance, nausea, constipation, urinary retention or incontinence, nocturia, impotence, and dry mucous membranes (Centers for Medicare & Medicaid Services, 2017).

An autonomic nervous system dysfunction that affects the cardiovascular system may result in either rapid resting or slowing heart rate. Blood pressure may drop on standing, a condition called “orthostatic hypotension.” Any cardiovascular effects may result in syncope, or loss of consciousness. An autonomic nervous system dysfunction affecting other organs may result in genitourinary symptoms (e.g., urinary incontinence, erectile dysfunction, or incomplete voiding/neurogenic bladder);
gastrointestinal symptoms (gastroparesis, diarrhea, or constipation); sweating problems with excessive or inadequate sweat production that can affect body temperature control; or vision difficulties from inappropriate pupillary constriction.

Many factors can cause autonomic nervous system neuropathy. Primary causes include familial dysautonomia (Riley-Day syndrome), idiopathic orthostatic hypotension (progressive autonomic failure), multiple system atrophy with autonomic failure (Shy-Drager syndrome), and Parkinson’s syndrome with autonomic failure. Over 1,000,000 Americans are impacted by a primary cause (Mayo Clinic, 2019). There are numerous secondary causes, including specific disorders such as diabetes mellitus, Lyme disease, and human immunodeficiency virus, or general dysfunctions such as physical trauma, surgery, pregnancy, or viral illness (Cleveland Clinic, 2016).

Autonomic neuropathy is an important, but not well-recognized complication of diabetes. Its clinical manifestations include orthostatic hypotension, exercise intolerance, gastroparesis, diarrhea, constipation, and urinary incontinence. The disorder is linked with sudden unexplained deaths in young people, even though the condition is relatively rare. In diabetic adults, autonomic neuropathy is a strong predictor of mortality, mostly due to cardiovascular disease, nephropathy, and hypoglycemia (Tang, 2013).

Autonomic nervous system testing includes three domains:

- **Cardiovagal innervation** is a test that provides a standardized quantitative evaluation of vagal innervation to parasympathetic function of the heart. Responses are based on the interpretation of changes in continuous heart recordings in response to standardized maneuvers and include heart rate response to deep breathing, Valsalva ratio, and 30:15 ratio heart rate responses to standing. A tilt table may be used, but is not required.

- **Vasomotor adrenergic innervation** evaluates adrenergic innervation of the circulation and of the heart in autonomic failure. The following tests are included: beat-to-beat blood pressure and R-R interval response to Valsalva maneuver, sustained hand grip, and blood pressure and heart rate responses to tilt-up or active standing and must be performed with a tilt table.

- **Sudomotor** is tests functions to evaluate and document neuropathic disturbances that may be associated with pain. The quantitative sudomotor axon reflex test, thermoregulatory sweat test, sympathetic skin responses, and silastic sweat imprints are tests of sympathetic cholinergic sudomotor function (Centers for Medicare & Medicaid Services, 2017).

**Searches**

Select Health of South Carolina searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality.
- The Centers for Medicare & Medicaid Services.
Cochrane reviews.

We conducted searches on February 13, 2019. Search terms were: “autonomic nervous system” and “neuropathy.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

The Centers for Medicare & Medicaid Services issued a Local Coverage Determination, effective November 2017, listing criteria (goals) for testing the autonomic nervous system and subsequent monitoring (Centers for Medicare & Medicaid Services, 2017). These criteria are specified in the coverage section of this policy.

An American Academy of Neurology practice parameter found that autonomic testing should be considered in evaluating patients with polyneuropathy to document autonomic nervous system involvement and suspected autonomic neuropathies. Both applications were given a level “B” grade by the expert panel (American Academy of Neurology, 2009).

A publication from the National Heart, Lung, and Blood Institute asserted that autonomic nervous system function is assessed by measuring resting heart rate, heart rate variability, or heart rate recovery after exercise. These measures can identify correlates of autonomic nervous system dysfunction for patients, such as obesity, diabetes, and heart failure (Lauer, 2009).

Recommendations from the Neuropathy Study Group of the Italian Society of Diabetology were produced because diabetic autonomic neuropathy is not often diagnosed. These recommendations include information on how and when to perform the recommended cardiovascular tests, and how to interpret them (Spallone, 2011).

Diabetic autonomic neuropathy is common among diabetics, and raises the morbidity and mortality risk in older adults as it often goes undiagnosed and untreated (Scheinberg, 2016). One study of 151 type 1 diabetes patients assessed the association of various risk factors to the disease. These included neuropathy and diabetic neuropathy; both were highly significant predictors of the disease (Tannus,
Another review found an under-diagnosis of cardiovascular autonomic neuropathy in persons with diabetes due to low interest in an unfamiliar complication, skepticism of therapies, lack of understanding diagnostic utility, and need for education and training — in spite of evidence of predictive value of neuropathy for the disease. A related issue is the lack of uniformity of treatment (Rolim, 2013).

A study of 490 persons ages 50 – 75 with diabetes followed for a median of 13.6 years found that cardiac autonomic dysfunction, described using 10 measures, was strongly associated with a risk of cardiovascular mortality. The study recommended such measures be monitored in persons with diabetes (Beijers, 2009). A related article found that the impact of hypoglycemia on cardiovascular autonomic function could explain the risk of cardiovascular mortality among persons with diabetes (Adler, 2009). Another study documented that more persons with diabetes on intensive therapy had neuropathy than those on standard therapy (Duckworth, 2009).

A systematic review of eight studies determined that heart rate variability is a reasonably effective tool in the diagnosis and prognosis of diabetes mellitus (sensitivity 72 – 100 percent, specificity 71 – 97 percent), and can be used as an adjunct to standard autonomic tests (Franca da Silva, 2016).

Risk factors for cardiac autonomic neuropathy were analyzed in a meta-analysis of four studies (n = 1,755). Factors that significantly raised risk included age, duration of diabetes, body mass index, proliferative retinopathy, microalbuminuria, hypertension, systolic and diastolic blood pressure, HbA1C, triglycerides, and high-density lipoprotein cholesterol. Findings allow practitioners to identify persons with diabetes at high risk of developing cardiac autonomic neuropathy (Dafaalla, 2016).

A systematic review of 18 (n = 6,915) retrospective and prospective cohort studies addressed monitoring of invasive and non-invasive heart rate variability — potentially a useful tool in addition to conventional autonomic tests — in intensive care units. Results included increases in mortality associated with reduction in variability (entropy 0.65 versus 0.84, \( P < .05 \)); reduction in the baroreflex (transfer) function (0.43 versus 1.11, \( P < .05 \)); sustained reduction of the low frequency/high frequency ratio (0.22 versus 0.62 \( P < .01 \)); loss of heart rate volatility during the first 24 hours of hospitalization; and reduction in variability in patients admitted to intensive care after cardiac arrest and undergoing therapeutic hypothermia (Bento, 2017).

A systematic review of 11 studies showed that documenting abnormal heart rate variability in patients with systemic lupus erythematosus have abnormal heart rate variability reflects cardiac autonomic dysfunction. Thus, heart rate can be a useful tool for monitoring autonomic dysfunction in the disease, and generate useful prognostic information (Matusik, 2018).

Individuals with metabolic syndrome have alterations in the function of the autonomic nervous system, and these alterations are linked with greater risk of aspects of the syndrome, such as obesity, hypertension, and insulin resistance — although the issue of whether these alterations are contributors or a consequence of the syndrome remains unresolved (Licht, 2010).
A review of 127 patients in 90 newly diagnosed type 2 diabetic patients and 37 patients with normal glucose tolerance were given Ewing tests and continuous glucose monitoring. The prevalence of cardiovascular autonomic neuropathy in newly-diagnosed diabetes was low (22.2 percent), while those with the greatest glycemic variability had the highest prevalence of cardiovascular autonomic neuropathy; thus glycemic variability can be a helpful method of identifying neuropathy (Xu, 2017).

Some new monitors have been developed to track autonomic nervous system activity. One pleth-wave derived parameter, the Perfusion Index, was tested on 20 patients, and index modifications occurred (Del Buono, 2016). Another monitor is a low-power, generic, small wireless sensor node to monitor physiological signals of responses of the autonomic nervous system (Brown, 2009).

Policy updates:

A total of three guidelines/other and three peer-reviewed references were added to, and one guideline/other and ten peer-reviewed references were removed from, the policy in February, 2019.

The Clinical Policy number was changed from #CP.09.01.01 to CCP.1005 in February, 2019.

References

Professional society guidelines/other:


InterQual®: CP: Autonomic function tests.


Cleveland Clinic. Autonomic Neuropathy or Autonomic Dysfunction (Syncope): Information and Instructions. https://my.clevelandclinic.org/health/diseases/15631-autonomic-neuropathy-or-


**Peer-reviewed references:**


**Centers for Medicare & Medicaid Services National Coverage Determinations:**

70.2.1 Services provided for the Diagnosis and Treatment of Diabetic Sensory Neuropathy with Loss of Protective Sensation (aka Diabetic Peripheral Neuropathy).

**Local Coverage Determinations:**

L35124 Autonomic Function Testing.

L35395 Autonomic Function Tests.

L36236 Autonomic Function Testing.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is
not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>95921</td>
<td>Testing of autonomic nervous system function, cardiovagal innervation (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>
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<tr>
<td>95922</td>
<td>Testing of autonomic nervous system function, vasomotor adrenergic innervation (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>
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<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>
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<tr>
<td>95924</td>
<td>Combined parasympathetic and sympathetic adrenergic function testing with at least 5 minutes of passive tilt</td>
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<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>
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<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>E08.43</td>
<td>Diabetes mellitus due to underlying condition with diabetic autonomic (poly)neuropathy</td>
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<tr>
<td>E08.49</td>
<td>Diabetes mellitus due to underlying condition with other diabetic neurological complication</td>
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<tr>
<td>E09.43</td>
<td>Drug or chemical induced diabetes mellitus with neurological complications with diabetic autonomic (poly)neuropathy</td>
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<td>E09.49</td>
<td>Drug or chemical induced diabetes mellitus with neurological complications with other diabetic neurological complication</td>
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<tr>
<td>E10.43</td>
<td>Type 1 diabetes mellitus with diabetic autonomic, (poly)neuropathy</td>
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<td>E10.49</td>
<td>Type 1 diabetes mellitus with other diabetic neurological complication</td>
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<td>E11.43</td>
<td>Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy</td>
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<td>E13.43</td>
<td>Other specified diabetes mellitus with diabetic autonomic (poly)neuropathy</td>
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<tr>
<td>G60.3</td>
<td>Idiopathic progressive neuropathy</td>
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<tr>
<td>G90.1</td>
<td>Familial dysautonomia (Riley-Day Syndrome)</td>
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<td>G90.2</td>
<td>Horner's syndrome</td>
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<td>ICD-10 Code</td>
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<td>G90.3</td>
<td>Shy-Drager Syndrome</td>
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<td>G90.4</td>
<td>Autonomic dysreflexia</td>
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<td>G90.8</td>
<td>Other disorders of autonomic nervous system</td>
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<td>G90.9</td>
<td>Disorder of the autonomic nervous system, unspecified</td>
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<td>G99.0</td>
<td>Autonomic neuropathy in diseases classified elsewhere</td>
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<td>R55</td>
<td>Syncope and collapse</td>
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