

Corporate Medical Policy

Autonomic Nervous System Testing

File Name: autonomic_nervous_system_testing

Origination: 3/2023

Last Review: 10/2024

Description of Procedure or Service

Autonomic Nervous System

The autonomic nervous system (ANS) has a primary role in controlling physiologic processes not generally under conscious control. They include heart rate, respirations, gastrointestinal (GI) motility, thermal regulation, bladder control, and sexual function. The ANS is a complex neural regulatory network that consists of two complementary systems that work to maintain homeostasis: the sympathetic and the parasympathetic systems. The sympathetic nervous system is responsible for arousal, and sympathetic stimulation leads to increased pulse, increased blood pressure (BP), increased sweating, decreased GI motility, and an increase in other glandular exocrine secretions. This is typically understood as the "fight or flight" response. Activation of the parasympathetic nervous system will mostly have the opposite effects: BP and pulse decrease, GI motility increases, and decreased sweating and other glandular secretions.

Autonomic Nervous System Disorders

Disorders of the ANS, also called dysautonomias, are heterogeneous in etiology, clinical symptoms, and severity. Autonomic nervous system disorders can be limited and focal, such as with isolated neurocardiogenic syncope or idiopathic palmar hyperhidrosis. At the other extreme, some ANS disorders can be widespread and severely disabling, such as multiple systems atrophy, which leads to widespread and severe autonomic failure.

Symptoms of autonomic disorders can vary based on the etiology and location of dysfunction. Cardiovascular manifestations are often prominent. Involvement of the cardiovascular system causes abnormalities in heart rate control and vascular dynamics. Orthostatic hypotension and other manifestations of BP lability can occur, causing weakness, dizziness, and syncope. Resting tachycardia and an inability to appropriately increase heart rate in response to exertion leads to exercise intolerance. There is a 2- to 3-fold higher incidence of major cardiac events in individuals with diabetic autonomic neuropathy, including myocardial infarction, heart failure, resuscitation from ventricular arrhythmia, angina, or the need for revascularization. There is also an increase in sudden cardiac death and overall mortality for these individuals.

Many other organ systems can be affected by autonomic neuropathy. Involvement of the bladder can lead to incomplete emptying, resulting in urinary retention and possible overflow incontinence. Gastrointestinal involvement is commonly manifested as gastroparesis, which is defined as slowed gastric emptying and can cause nausea, vomiting, and a decreased tolerance for solid food and large meals. Constipation may also occur if the lower GI tract is involved. Impairment of sexual function in males can manifest as erectile dysfunction and ejaculatory failure. Dysfunction of thermal regulation and sweating can lead to anhidrosis and heat intolerance. Paradoxically, excessive sweating can also occur as a compensatory mechanism in unaffected regions.

A classification of the different types of autonomic dysfunction, adapted from Freeman (2005) and Macdougall and McLeod (1996), can be made as follows:

Autonomic Nervous System Testing

- Diabetic autonomic neuropathy
- Amyloid neuropathy
- Immune-mediated neuropathy
 - Rheumatoid arthritis
 - Systemic lupus erythematosus
 - Sjögren syndrome
- Paraneoplastic neuropathy
- Inflammatory neuropathy
 - Guillain-Barré syndrome
 - Chronic inflammatory demyelinating polyneuropathy
 - Crohn disease
 - Ulcerative colitis
- Hereditary autonomic neuropathies
- Autonomic neuropathy secondary to infectious disease
 - HIV disease
 - Lyme disease
 - Chagas disease
 - Diphtheria
 - Leprosy
- Acute and subacute idiopathic autonomic neuropathy
- Toxic neuropathies.

Other chronic diseases may involve an ANS imbalance, without outright dysfunction of the nerves themselves. Approximately 40% of individuals with essential hypertension will show evidence of excess sympathetic activity. Sympathetic overactivity is also a prominent feature of generalized anxiety, panic disorder, and some types of depression, as well as certain cardiac disorders such as chronic heart failure. These types of ANS imbalances are not usually classified as ANS disorders.

Treatment of Autonomic Nervous System Disorders

Much of the treatment for autonomic disorders is nonpharmacologic and supportive. However, there are specific actions that can improve symptoms in individuals with specific deficits. For individuals with orthostatic hypotension, this involves adequate intake of fluids and salt, moving to an upright position slowly and deliberately, use of lower-extremity compression stockings, and keeping the head of the bed elevated 4 to 6 inches (ie, 10-15 cm). In severe cases, medications that promote salt retention, such as fludrocortisone, are often prescribed. Individuals with symptoms of hyperhidrosis may benefit from cooling devices and potent antiperspirants such as Drysol™, and individuals with decreased tearing and dry mucous membranes can use over-the-counter artificial tears or other artificial moisturizers.

Autonomic Nervous System Testing

Autonomic nervous system testing consists of a battery of tests intended to evaluate the integrity and function of the ANS. Any single test may be performed individually, or the entire battery of tests may be ordered. Individual components of testing may include cardiovascular function testing, sudomotor function, salivation testing, and tilt table testing. These tests are intended as adjuncts to clinical examination in the diagnosis of ANS disorders.

Cardiovascular Function Testing

Beat-to-beat variability in the heart rate can be measured at rest, or in response to provocative measures, such as deep breathing or the Valsalva maneuver. Reduced or absent heart rate variability is a sign of autonomic dysfunction.

Baroreflex sensitivity is measured by examining the change in pulse and heart rate variability in response to changes in BP. A medication such as phenylephrine is given to induce a raise in BP,

Autonomic Nervous System Testing

and baroreflex sensitivity is calculated as the slope of the relation between heart rate variability and BP.

Sudomotor Function (Sweat Testing)

Sweat testing evaluates the structure and function of nerves that regulate the sweat glands.

The Quantitative Sudomotor Axon Reflex Test is an example of a commercially available semiquantitative test of sudomotor function. The test is performed by placing the color-sensitive paper on the skin, which changes color on contact with sweat. Measurement of the amount of color change is a semiquantitative measure of sudomotor function.

For the silastic sweat imprint, silastic material is placed on the skin, and the sweat droplets form indentations on the silastic surface, allowing quantitation of the degree of sweating present. The Neuropad® test is an example of a commercially available silastic sweat imprint.

A more complex approach in some centers is the use of a thermoregulatory laboratory. This is a closed chamber in which an individual sits for a defined period under tightly controlled temperature and humidity. An indicator dye is brushed on the skin, and it changes color when in contact with sweat. Digital pictures are taken and projected onto anatomic diagrams. Computer processing derives values for a total area of anhidrosis and the percent of anhidrotic areas.

Sympathetic skin response tests use an electric current to stimulate sympathetic nerves. The tests measure the change in electrical resistance, which is altered in the presence of sweat. In general, these tests are considered to be sensitive but have high variability and potential for false-positive results.

A variant of sympathetic skin response testing is electrochemical sweat conductance measured by iontophoresis (e.g., Sudoscan®). In this test, a low-level current is used to attract chloride ions from sweat glands. The chloride ions interact with stainless-steel plate electrodes to measure electrochemical resistance.

Salivation Testing

The protocol for salivation testing involves the subject chewing on a preweighed gauze for 5 minutes. At the end of 5 minutes, the gauze is removed and reweighed to determine the total weight of saliva present.

Tilt Table Testing

Tilt table testing is intended to evaluate for orthostatic intolerance. The individual lies on the table and is strapped in with a footrest. The table is then inclined to the upright position, with monitoring of the pulse and BP. Symptoms of lightheadedness or syncope in conjunction with changes in pulse or BP constitute a positive test. A provocative medication, such as isoproterenol, can be given to increase the sensitivity of the test.

Composite Autonomic Severity Score

The Composite Autonomic Severity Score, which ranges from 0 to 10, is intended to estimate the severity of autonomic dysfunction. Scores are based on self-reported symptoms measured by a standardized symptom survey. Scores of 3 or less are considered mild, scores of 3 to 7 are considered moderate, and scores greater than 7 are considered severe. Autonomic nervous system testing consists of tests in three categories:

- Cardiovascular function (heart rate variability, heart rate response to deep breathing, and Valsalva maneuver)
- Vasomotor adrenergic function (blood pressure response to standing, Valsalva maneuver, hand grip, and tilt table testing)

Autonomic Nervous System Testing

- Sudomotor function (Quantitative Sudomotor Axon Reflex Test, quantitative sensory test, Thermoregulatory Sweat Test, silastic sweat imprint, sympathetic skin response, and electrochemical sweat conductance).

At least one test in each category is usually performed. More than one test from a category will often be included in a battery of tests, but the incremental value of using multiple tests in a category is unknown.

There is little evidence on the comparative accuracy of different ANS tests, but the following tests are generally considered to have uncertain value in ANS testing:

- Pupillography
- Pupil edge light cycle
- Gastric emptying tests
- Cold pressor test
- Quantitative direct and indirect testing of sudomotor function test
- Plasma catecholamine levels
- Skin vasomotor testing
- The ANSAR test.

Regulatory Status

Since 1976, numerous ANS testing devices have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Examples are listed below.

- ANX 3.0
- Sudoscan
- Hrv Acquire
- ZYTO Hand Cradle
- Bodytronic® 200
- Finapres® Nova Noninvasive Hemodynamic Monitor
- VitalScan® ANS

The Neuropad test (TRIGOCare) is another example of a commercially available sudomotor function test. No records were identified indicating that Neuropad has been cleared for marketing by the U.S. FDA.

Related Policies:

Neural Therapy

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for Autonomic Nervous System Testing when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Autonomic Nervous System Testing

When Autonomic Nervous System Testing is covered

Autonomic nervous system testing, consisting of a battery of tests in several domains (see Policy Guidelines section), may be considered **medically necessary** when the following criteria are met:

- Signs and/or symptoms of autonomic dysfunction are present; AND
- A definitive diagnosis cannot be made from clinical examination and routine laboratory testing alone; AND
- Diagnosis of the suspected autonomic disorder will lead to a change in management or will eliminate the need for further testing.

When Autonomic Nervous System Testing is not covered

Autonomic nervous system testing is considered **investigational** in all other situations when criteria are not met, including but not limited to the evaluation of the following conditions:

- Chronic fatigue syndrome
- Fibromyalgia
- Anxiety and other psychologic disorders
- Sleep apnea
- Allergic conditions
- Hypertension
- Screening of asymptomatic individuals
- Monitoring progression of disease or response to treatment.

Autonomic nervous system testing using portable automated devices is considered **investigational** for all indications (see Policy Guidelines section).

Policy Guidelines

Although there is no standard battery of tests for autonomic nervous system (ANS) testing, a full battery generally consists of individual tests in three categories.

- Cardiovascular function (heart rate variability, heart rate response to deep breathing, and Valsalva maneuver)
- Vasomotor adrenergic function (blood pressure response to standing, Valsalva maneuver, hand grip, and tilt table testing)
- Sudomotor function (Quantitative Sudomotor Axon Reflex Test, quantitative sensory test, Thermoregulatory Sweat Test, silastic sweat imprint, sympathetic skin response, and electrochemical sweat conductance).

Autonomic Nervous System Testing

At least one test in each category is usually performed. More than one test from a category will often be included in a battery of tests, but the incremental value of using multiple tests in a category is unknown.

There is little evidence on the comparative accuracy of different ANS tests, but the following tests are generally considered to have uncertain value in ANS testing:

- Pupillography
- Pupil edge light cycle
- Gastric emptying tests
- Cold pressor test
- Quantitative direct and indirect testing of sudomotor function test
- Plasma catecholamine levels
- Skin vasomotor testing
- The ANSAR® test.

Autonomic nervous system testing should be performed in a dedicated ANS testing laboratory. Testing in a dedicated laboratory should be performed under closely controlled conditions, and results should be interpreted by an individual with expertise in ANS testing. Testing using automated devices with results interpreted by computer software has not been validated and thus has the potential to lead to erroneous results.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 95921, 95922, 95923, 95924

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Gibbons CH, Cheshire WP, Fife TD. American Academy of Neurology Model Coverage Policy: Autonomic Nervous System Testing. 2014; https://www.aan.com/siteassets/home-page/tools-and-resources/practicing-neurologist--administrators/billing-and-coding/model-coverage-policies/14autonomicmodel_tr.pdf. Accessed February 16, 2023.

Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. *Circulation*. Jan 23 2007; 115(3): 387-97. PMID 17242296

England JD, Gronseth GS, Franklin G, et al. Practice Parameter: evaluation of distal symmetric polyneuropathy: role of autonomic testing, nerve biopsy, and skin biopsy (an evidence-based

Autonomic Nervous System Testing

review). Report of the American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation. *Neurology*. Jan 13 2009; 72(2): 177-84. PMID 19056667

Bellavere F, Ragazzi E, Chilelli NC, et al. Autonomic testing: which value for each cardiovascular test? An observational study. *Acta Diabetol*. Jan 2019; 56(1): 39-43. PMID 30159748

Park JY, Yang D, Yang HJ, et al. Quantitative autonomic function test in differentiation of multiple system atrophy from idiopathic Parkinson disease. *Chin Med J (Engl)*. Aug 20 2019; 132(16): 1919-1924. PMID 31373907

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*. Feb 2021; 132(2): 666-682. PMID 33419664

Policy Department, American Association of Neuromuscular & Electrodiagnostic Medicine, Rochester, Minnesota, USA. Proper performance of autonomic function testing. *Muscle Nerve*. Jan 2017; 55(1): 3-4. PMID 27786371

Klein CM. Evaluation and management of autonomic nervous system disorders. *Semin Neurol*. Apr 2008; 28(2): 195-204. PMID 18351521

Valensi P, Sachs RN, Harfouche B, et al. Predictive value of cardiac autonomic neuropathy in diabetic patients with or without silent myocardial ischemia. *Diabetes Care*. Feb 2001; 24(2): 339-43. PMID 11213889

Freeman R. Autonomic peripheral neuropathy. *Lancet*. Apr 2005; 365(9466): 1259-70. PMID 15811460

McDougall AJ, McLeod JG. Autonomic neuropathy, II: Specific peripheral neuropathies. *J Neurol Sci*. Jun 1996; 138(1-2): 1-13. PMID 8791232

Goldstein DS, Robertson D, Esler M, et al. Dysautonomias: clinical disorders of the autonomic nervous system. *Ann Intern Med*. Nov 05 2002; 137(9): 753-63. PMID 12416949

Low PA. Testing the autonomic nervous system. *Semin Neurol*. Dec 2003; 23(4): 407-21. PMID 15088262

Specialty Matched Consultant Review 10/2023

Medical Director Review 10/2023

TRIGOCare International GmbH. Neuropad: Diagnostic test for sudomotor dysfunction and early detection of diabetic foot syndrome, diabetic neuropathy. 2014; <https://www.neuropad.com/>.

Specialty Matched Consultant Review 10/2024

Medical Director Review 10/2024

Autonomic Nervous System Testing

Policy Implementation/Update Information

- 5/30/23 New policy developed. Autonomic nervous system (ANS) testing may be considered medically necessary when criteria are met. ANS testing using portable, automated devices is considered investigational. Medical Director review. Notification given 5/30/2023 for effective date 8/1/2023. (sk)
- 11/7/23 References updated. Added related policy. Updated listing of U.S. FDA approved ANS testing devices. Specialty Matched Consultant Review 10/2023. Medical Director review 10/2023. (ldh)
- 11/13/24 References updated. Specialty Matched Consultant Review 10/2024. Medical Director review 10/2024. (ldh)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.