Autonomic Nervous System Testing

Description

The autonomic nervous system (ANS) controls physiologic processes that are not under conscious control.

ANS Testing

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

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

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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.

Sym pathetic 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 (eg, 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 patient lies on the table and is strapped in with a foot rest. 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.

OBJECTIVE

The objective of this evidence review is to determine whether ANS testing improves the net health outcome in patients with a suspected autonomic disorder.

POLICY STATEMENT

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.

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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 3 categories.

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

At least 1 test in each category is usually performed. More than 1 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.

ANS 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.

**BENEFIT APPLICATION**

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

**FDA REGULATORY STATUS**

Since 1976, numerous ANS testing devices have been cleared for marketing by the US Food and Drug Administration through the 510(k) process. Table 1 lists examples.
Table 1. Autonomic Nervous System Test Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Measurement</th>
<th>510(k) No.</th>
<th>Clearance Date</th>
<th>Product Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANX 3.0</td>
<td>Ansar Group</td>
<td>Respiration and heart rate variability</td>
<td>K941252</td>
<td>2004</td>
<td>DRT</td>
</tr>
<tr>
<td>Sudoscan</td>
<td>Impeto Medical</td>
<td>Electrochemical sweat conductance</td>
<td>K100233</td>
<td>2010</td>
<td>GZO</td>
</tr>
<tr>
<td>ZYTO Hand Cradle</td>
<td>ZYTO Technologies</td>
<td>Galvanic skin response</td>
<td>K111308</td>
<td>2011</td>
<td>GZO</td>
</tr>
<tr>
<td>Bodytronic 200</td>
<td>Bauerfeind</td>
<td>Photoelectric plethysmograph</td>
<td>K123921</td>
<td>2013</td>
<td>JMO</td>
</tr>
<tr>
<td>Neuropad</td>
<td>TRIGOcare</td>
<td>Sudomotor function</td>
<td></td>
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</tbody>
</table>

**RATIONALE**

### Summary of Evidence

For individuals who have signs and symptoms of ANS dysfunction who receive ANS testing, the evidence includes studies of diagnostic accuracy. Relevant outcomes are test accuracy, symptoms, functional outcomes, and quality of life. The evidence base is limited. There is a lack of a criterion standard for determining autonomic dysfunction, which limits the ability to perform high-quality research on diagnostic accuracy. Also, numerous tests are used in various conditions, making it difficult to determine values for the overall diagnostic accuracy of a battery of tests. Scattered reports of diagnostic accuracy are available for certain tests, most commonly in the diabetic population, but these reports do not specify estimates of accuracy for the entire battery of tests. Reported sensitivities and specificities are high for patients with clinically defined distal symmetric polyneuropathy using a symptom-based score as a reference standard, but these estimates are likely biased by study designs that used patients with clinically diagnosed disease and a control group of healthy volunteers. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

### Practice Guidelines and Position Statements

Evidence-based guidelines on autonomic nervous system (ANS) testing are lacking. Even in guidelines that involve a systematic review of the literature, such as the joint American Academy of Neurology (AAN), American Association of Neuromuscular & Electromyography (AANEM), and the American Academy of Physical Medicine & Rehabilitation guidelines (described below), recommendations were largely based on expert consensus.

**American Academy of Neurology et al**

AAN, AANEM, and American Academy of Physical Medicine & Rehabilitation (2009) issued a practice parameter, affirmed in July 2013, on the evaluation of distal symmetric polyneuropathy. This document addressed the use of autonomic testing in the evaluation of patients with distal symmetric polyneuropathy. The following conclusion and recommendations were made:

*Autonomic testing is probably useful in documenting autonomic nervous system involvement in polyneuropathy (Class II and Class III). The sensitivity and specificity vary with the particular test. The utilization of the combination of autonomic reflex screening tests in the CASS [Composite Autonomic Severity Score] probably provides the highest sensitivity and specificity for documenting autonomic dysfunction (Class II).*

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Autonomic testing should be considered in the evaluation of patients with polyneuropathy to document autonomic nervous system involvement (Level B).

Autonomic testing should be considered in the evaluation of patients with suspected autonomic neuropathies (Level B) and may be considered in the evaluation of patients with suspected distal SFSN [small fiber sensory neuropathy] (Level C).

The combination of autonomic screening tests in the CASS should be considered to achieve the highest diagnostic accuracy (Level B).

American Association of Neuromuscular and Electrodiagnostic Medicine

AANEM (2017) published a position statement on the proper performance of autonomic function testing. AANEM recommended that:

- "Autonomic testing procedures be performed by physicians with comprehensive knowledge of neurologic and autonomic disorders to ensure precise interpretation and diagnosis at completion of testing," and that
- "The same physician should directly supervise and interpret the data on-site...", and
- "It is inappropriate to interpret autonomic studies without obtaining a relevant history to understand the scope of the problem, obtaining a relevant physical examination to support a diagnosis, and providing the necessary oversight in the design and performance of testing."

American Academy of Neurology

AAN published a model coverage policy on autonomic testing in 2014. The document addressed:

- The qualifications of physicians who perform ANS testing.
- Techniques used in ANS testing.
- The types of patients who will benefit from ANS testing.
- The clinical indications for testing.
- Diagnoses where testing is indicated.
- Indications for which data are limited.

American Diabetes Association

The American Diabetes Association (2010) published standards of care for treatment in diabetes. This document contained the following statements on autonomic neuropathy in diabetes (where E is expert opinion):

- "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 outcome (E).
- Medications for the relief of specific symptoms related to DPN [distal polyneuropathy] and autonomic neuropathy are recommended, as they improve the quality of life of the patient (E)."

European Society of Cardiology

The European Society of Cardiology (2017) published a position statement on potential treatments for dysfunction of the autonomic nervous system in context of heart failure. The statement cited some noninvasive ANS tests, such as standing, deep breathing, and Valsalva's maneuvers, but noted that none of these has shown "prognostic importance."

European Federation of Neurological Societies

The European Federation of Neurological Societies (2011) issued a revision of its guidelines on orthostatic hypotension. The guidelines made a level C recommendation that ANS screening tests with other appropriate investigations should be considered depending on the possible etiology of the underlying disorder.
U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


FEP 2.01.96 Autonomic Nervous System Testing


**POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2015</td>
<td>New policy</td>
<td>Policy created with literature review through July 24, 2014; clinical input reviewed. Autonomic nervous system (ANS) testing may be considered medically necessary when criteria are met. ANS testing using portable, automated devices is considered not medically necessary.</td>
</tr>
<tr>
<td>September 2018</td>
<td>Replace policy</td>
<td>Policy updated with literature review through April 8, 2018; reference 15, 17 and 20 added; reference 18 updated. Policy statements unchanged except “not medically necessary” corrected to “investigational” due to FDA 510(k) clearance.</td>
</tr>
<tr>
<td>September 2019</td>
<td>Replace policy</td>
<td>Policy updated with literature review through April 1, 2019; reference added. Policy statements unchanged.</td>
</tr>
</tbody>
</table>

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