# All India Institute of Medical Sciences Rajkot

## *Clinical Applications of Autonomic Function Tests(AFT)*

**e – Bulletin**

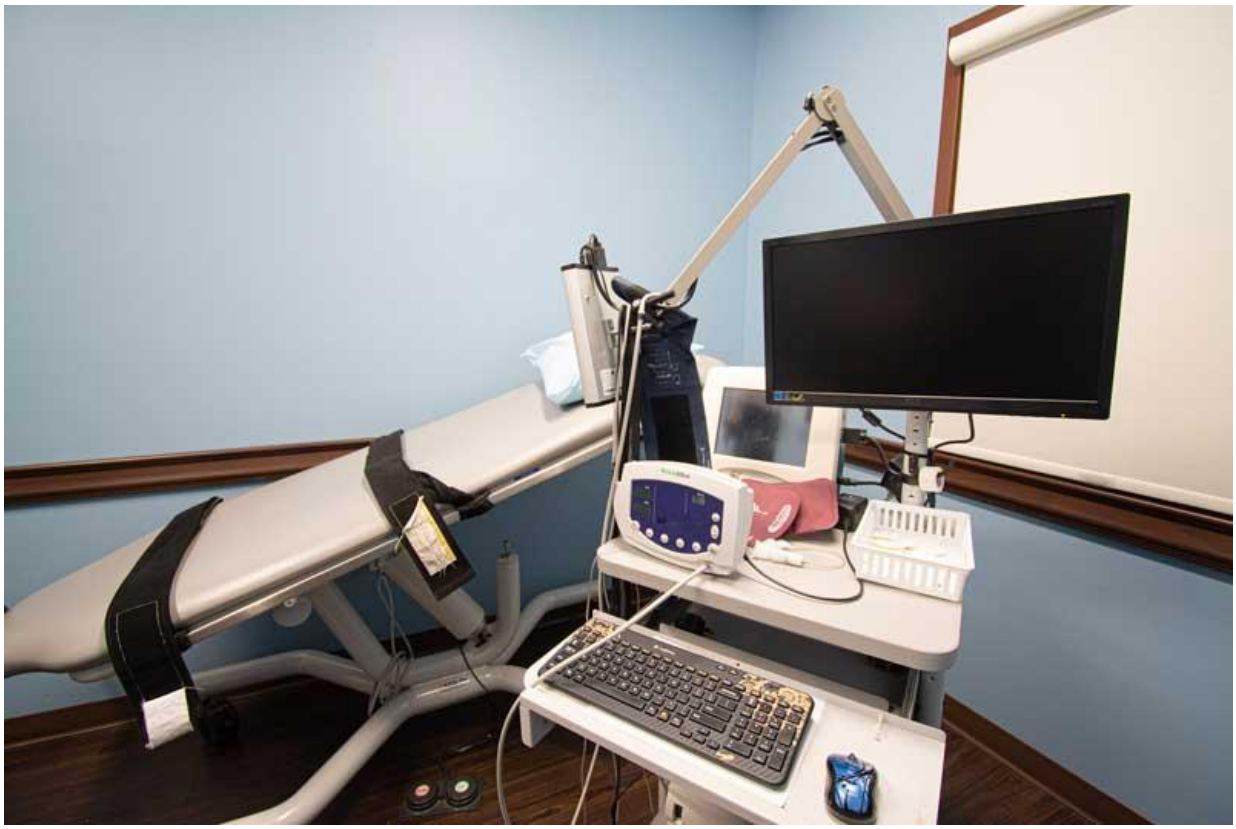
Published by

Department of Physiology

All India Institute of Medical Sciences (AIIMS), Rajkot

## AN INTRODUCTION TO AUTONOMIC FUNCTION TESTING

The autonomic function testing (AFT) refers to the evaluation of the sympathetic, and parasympathetic division of autonomic nervous systems (ANS). The system affects function of almost every organ system in the body; hence, many tests that seem unique to a particular organ are really tests of autonomic function (e.g., urodynamic studies, gastric motility testing, pupillometry, tests of salivary and lacrimal gland secretion, etc.). Through scientific research and clinical experience published in peer-reviewed journals, autonomic function testing has proven its worth in the diagnosis and treatment of autonomic disorders over the past many years. Autonomic testing is now considered as a crucial part of the clinical assessment.





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## COMMON TERMS IN AUTONOMIC TESTING

**Autonomic Nervous System:** The part of the nervous system that controls involuntary visceral actions.

**Cardiovagal:** The parasympathetic response measured via cardiac function, which is under control of the vagus nerve, which influences heart rate variability.

**Heart Rate Variability:** A test of parasympathetic function in which an individual undergoes a standard series of breathing exercises and the variability in the heart rate response is measured. *Diminished heart rate variability* (diminished respiratory sinus arrhythmia) is a sign of parasympathetic dysfunction.

**Quantitative Sudomotor Axon Reflex Test (QSART):**

A test to evaluate the integrity of postganglionic sudomotor nerve along the axon reflex to define the volume and distribution of sweat loss. This is accomplished by releasing acetylcholine into the skin, which activates distal postganglionic sudomotor nerves, which then activates receptors on the eccrine sweat gland. The sweat response is typically recorded from four sites (one forearm and three lower extremity sites) and the waveforms generated are assessed for deficits.

**Sudomotor:** The sympathetic cholinergic component of the autonomic nervous system is responsible for sweat gland function and the production of thermoregulatory sweating.

**Sympathetic Skin Response:** A test to measure a provoked change in the electrical potential of the skin.

**Thermoregulatory Sweat Test (TST):** A test of sweat function and its neurologic regulation in which a generalized thermoregulatory sweating response is elicited by raising the core body temperature and monitoring sweat production by an indicator dye applied to the skin of the whole body. TST investigates the integrity of the central and peripheral thermoregulatory sympathetic pathways. Digital photography is used to document the sweat distribution, which can be characteristic of neuropathy, ganglionopathy, or generalized autonomic failure.

**Valsalva Maneuver:** An autonomic testing maneuver in which the patient exhales against resistance and the blood pressure and heart rate are recorded, typically on a beat-to-beat basis. This test evaluates the complex sympathetic adrenergic and parasympathetic responses to the transient reduction in cardiac preload caused by an increase in intrathoracic pressure.



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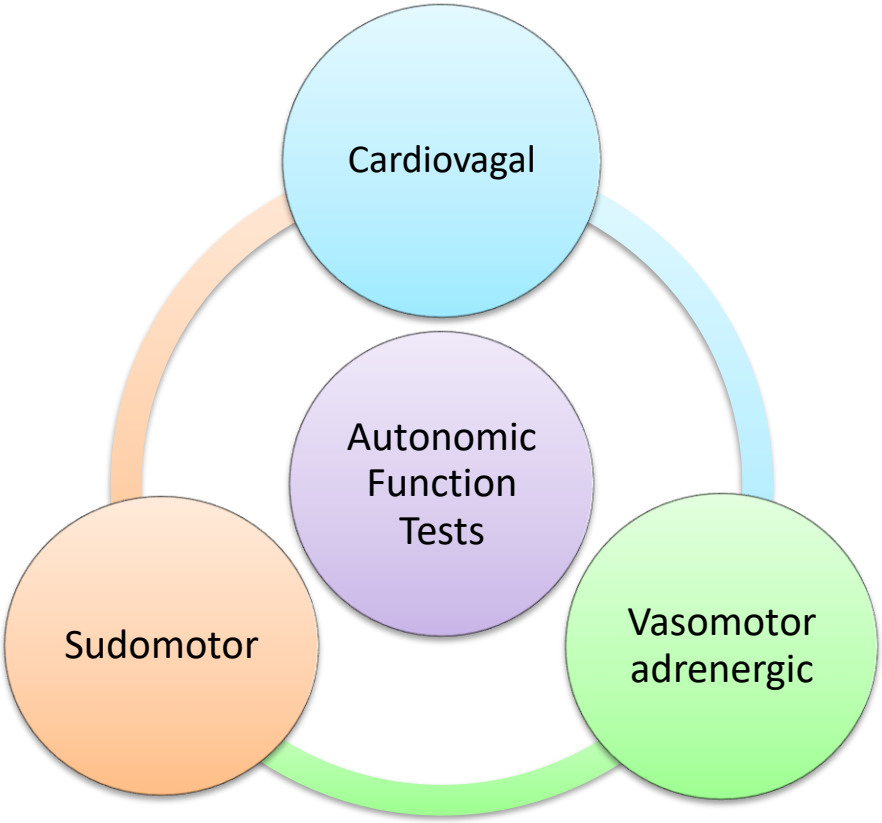
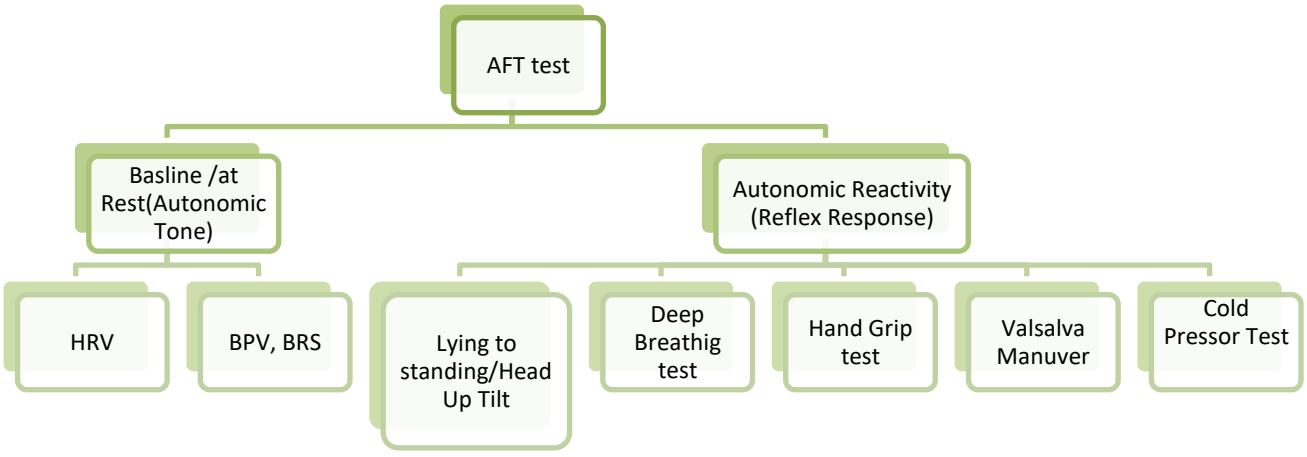
## TECHNIQUES USED IN AUTONOMIC TESTING




### A. *Cardiovagal Autonomic Testing*:

Autonomic nervous system modulates heart rate mainly through the vagus nerve. This modulation is tested in two conditions of physiological systems



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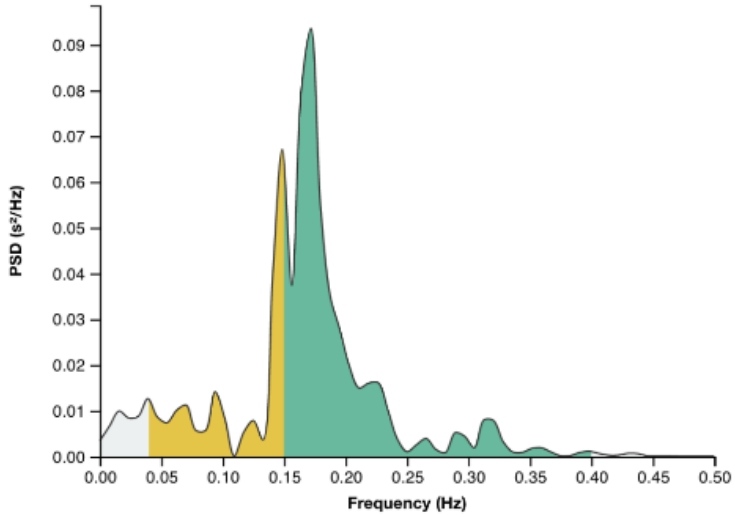
1. Autonomic Tone

    a. **Heart rate variability (HRV)** is a simple and reliable test of cardiovagal function. It has a sensitivity of 97.5 percent for detecting parasympathetic dysfunction in diabetes when age-adjusted normative values are used.

        i. Time domain Analysis: statistical analysis of beat to beat interval of resting HR
            1. RMSSD
            2. NN50
            3. pNN50

        ii. Frequency Domain Analysis: Fast Fourier Analysis(FFT) of beat to beat interval of resting HR

            1. High frequency (HF) : absolute and normalized units
            2. Low frequency (LF): absolute and normalized units
            3. LF/HF ratio
            4. Total power




    b. **Blood pressure Variability (BPV) and Baroreflex sensitivity (BRS)** also used to measure control of cardiovascular reflexes by ANS.

2. A***utonomic reactivity Parameters: Parasympathetic***

    i. **Heart rate response to deep breathing**. participants will be comfortably lying supine, and ECG and respiratory events will be recorded. Subjects will be asked to breathe deeply at a rate of 6 breaths/min, followed by slow and deep expiration. Changes in HR between inspiration and expiration will be averaged over six cycles. This test approaches the optimal test for cardiovagal function. Both the afferent and efferent pathways are vagal. The end point is the maximal HR variability obtained under laboratory conditions, where the confounding variables of age, rate, and depth of respiration were controlled.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ii. **Valsalva ratio**: participants will be asked to sit on a chair. Their nostrils will be closed with a nose clip, and a mouthpiece will be placed into the mouth and connected to a manometer. The recording will be taken on the ECG machine, and then the participants will be asked to breathe forcefully into the mercury manometer and maintain the expiratory pressure at 40 mmHg for 10-15 seconds. The ECG will be recorded during the maneuver and 45 seconds after the maneuver. This ratio is derived from the maximal HR generated by the Valsalva maneuver divided by the lowest HR following the maneuver.

iii. **Heart rate response to standing**. The initial HR responses to standing consist of a tachycardia at 3 then 12 seconds followed by a bradycardia at 20 seconds. The initial cardioacceleration is an exercise reflex, while the subsequent tachycardia and bradycardia are baroreflex mediated. participants will be asked to lie supine, fully relaxed on a couch for 10 minutes. ECG will be recorded, and basal HR will be calculated. Subsequently, the participants will be instructed to stand up immediatelyThe 30:15 ratio (R-R interval at beat 30)/(R-R interval at beat 15), has been recommended as an index of cardiovagal function.

### B. *Vasomotor Adrenergic Autonomic Testing: Sympathetic*

Testing sympathetic adrenergic function is the primary method for evaluating patients with syncope, orthostatic hypotension, postural tachycardia syndrome, and postural dizziness. Such testing is sensitive, specific, and clinically useful to aid in diagnosis, management, and outcomes in patients with autonomic dysfunction or syncope of unexplained cause. Sympathetic adrenergic testing, when normal, is clinically useful also in ruling out autonomic failure when the history and bedside examination alone are diagnostically insufficient.

1. **Beat-to-beat BP recordings of the Valsalva maneuver**. The availability of a well-validated photoplethysmography volume clamp technique to measure beat-to-beat BP has permitted the application of the well-known properties of the phases of the Valsalva maneuver to the clinical laboratory.

2. **Sustained hand grip**. Sustained muscle contraction causes a rise in systolic and diastolic BP and HR. The stimulus derives from exercising muscle and central command. Efferent fibers travel to the muscle and heart, resulting in increased cardiac output, BP, and HR.

   Participants will be allowed to rest in a quiet room for 10 minutes before their resting BPs are measured by the auscultatory method using a mercury sphygmomanometer. Instructions will be given to the subjects to perform (dominant hand) hand grip in a dynamometer, giving as much pressure as they can apply for 3-4 seconds, which is the maximum voluntary contraction followed by sustained hand grip exercise, maintaining a pressure of 30% of maximum activity for 5 minutes with the dynamometer. BP will be recorded at this time and again after 5 minutes after completion of the exercise. The difference between the diastolic BP before and after the exercise will be considered the response.



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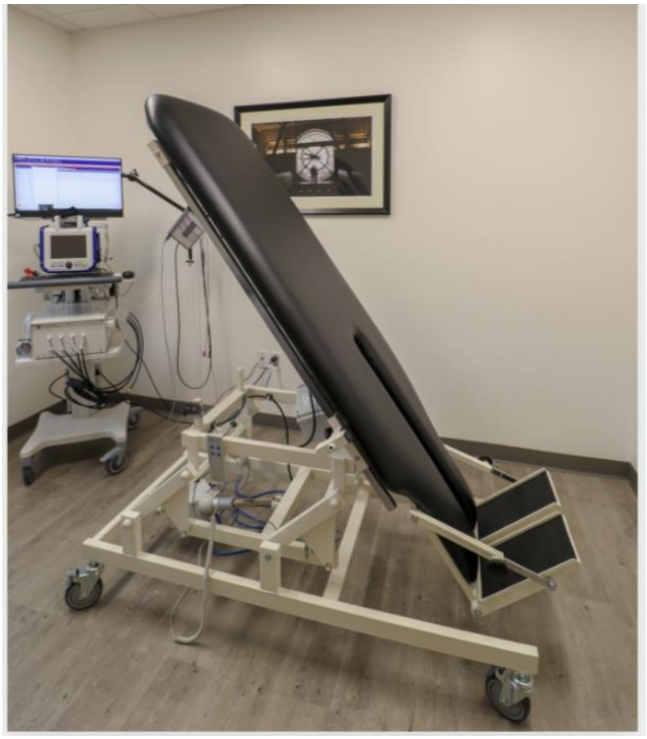
3. **Blood pressure and heart rate response to standing.**
   The subject will be asked to rest and then with the help of the Head up tilt (HUT) table, a challenge of head-up tilt of $90^0$ will be given to the subject and a change in blood pressure will be recorded immediately after HUT and then every minute for 5 minutes and then taken back to supine position and measured BP at for 2 minutes for every 1 minute. Supine and tilted BP recordings, especially when supplemented with beat-to-beat BP and HR recordings, can be used as an established test of adrenergic function and are an essential part of any laboratory evaluation of patients with suspected adrenergic failure.



4. **Cold Pressure Test:** Basal BP of the participants will be recorded before they are asked to submerge one of their upper limbs in cold water (temperature at 2-4°C) kept in a pot for 1 minute. Their BPs will be recorded at 30 and 60 seconds of submersion of the limb.

## *C. Sudomotor Testing:*

Data from a considerable body of literature indicate that sudomotor testing may be the most sensitive means to detect a peripheral small fiber neuropathy.

1. **Quantitative sudomotor axon reflex test distribution**. The QSART measures axon reflex-mediated sudomotor responses quantitatively and evaluates postganglionic sudomotor function. Typically, recording from the forearm and lower extremities at three skin sites are used to assess the distribution of postganglionic deficits.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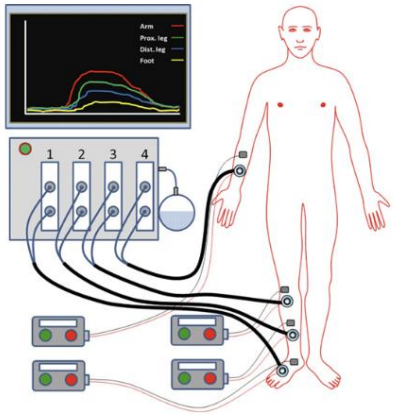
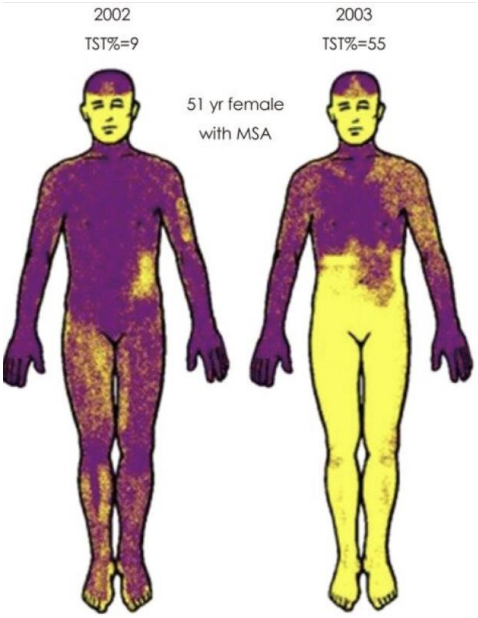
## Sudomotor Axon Reflex Test (QSART)




2. **Thermoregulatory sweat test**. The TST is now well-standardized. It evaluates the distribution of sweating by a change in the color of an indicator powder. The test has recently been rendered semiquantitative and expressed as a percentage of anterior body anhidrosis. The test has a high sensitivity. As a stand-alone test, it has a low specificity, and limited information on its reproducibility and confounding variables is available. Combined with QSART, its specificity for delineating the site of the lesion is greatly enhanced.




3. **Sympathetic skin responses**. The recorded skin potential is derived from activated eccrine sweat glands, and the amplitude and configuration are modulated by sweat gland epithelium and the overlying epidermis. The test is of relatively low sensitivity and uncertain specificity and habituates. Its greatest advantage is its relative ease of performance in a standard EMG laboratory.

4. **Sweat imprint**. This is formed by the secretion of active sweat glands into a plastic imprint. This test can be used to determine sweat gland density; a histogram of sweat droplet size and sweat volume per area can be obtained. The test seems to be sensitive and quantitative.



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## WHAT TYPES OF PATIENTS WILL BENEFIT FROM AUTONOMIC TESTING?

The American Diabetes Association (ADA) recommends that autonomic testing (including cardiovagal testing) be performed for all patients with *type 2 diabetes mellitus* at the time of *diagnosis and five years* after diagnosis in individuals with type 1 diabetes. Those recommendations are based on evidence showing that individuals with diabetes that have evidence of cardiac *autonomic neuropathy* have significantly *higher rates of mortality and silent myocardial ischemia*. Consensus on the usefulness of tests of autonomic function exists for a number of disorders and conditions. These tests, in general, are definable in terms of their ability to diagnose a condition, to provide unique differential diagnostic information, or to quantify those aspects of autonomic function that have an impact on outcome or evaluate treatment efficacy.

1. **Progressive autonomic neuropathy**. The role of autonomic testing in a patient suspected of having a progressive autonomic neuropathy is to diagnose the presence of autonomic neuropathy and determine its severity and distribution. It is possible to delineate the severity, involvement by autonomic system (cardiovagal, adrenergic, sudomotor), distribution, and level (pre- versus postganglionic) of autonomic failure.

2. **Differentiation of benign from life-threatening autonomic disorders**. Certain autonomic disorders mimic the more malignant generalized autonomic disorders. For instance, chronic idiopathic anhidrosis, a restricted autonomic disorder with a good prognosis, is diagnosable only by excluding adrenergic and cardiovagal failure. The differential diagnosis between certain complicated variants of syncopes from other causes of loss of consciousness may require autonomic tests. Similarly, when the response to β-receptor blockade might be inadequate in vasodepressor syncope, autonomic studies are needed, because the lack of response might be due to peripheral autonomic failure.

3. **Distal small fiber neuropathy**. This neuropathy is common, often distressing, and very difficult to diagnose. Routine nerve conduction studies and EMG are usually normal, as the brunt of the disorder is on unmyelinated fibers. The QSART or the TST is abnormal in approximately 80% of cases. For the patient who has distressing symptoms, autonomic studies are indicated, since this might be the only means of diagnosing the condition, and will often obviate the need for expensive investigations such as spinal MRI.

4. **Postural tachycardia syndrome**. Patients with postural tachycardia syndrome may have an autonomic neuropathy. The orthostatic tachycardia might be due to hypovolemia, peripheral adrenergic failure with preservation of cardiac autonomic innervation, β-receptor supersensitivity, or an abnormality in brain stem regulation An autonomic screen is necessary to clarify this differential diagnosis.

5. **Sympathetically maintained pain.** Patients with unilateral limb pain in whom the suspicion of sympathetically maintained pain, as in reflex sympathetic dystrophy or causalgia, will have sympathetic overaction. Sympathetic overaction may also occur as a manifestation of augmented somatosympathetic reflexes. It is possible to use autonomic tests to demonstrate asymmetry of vasomotor and sudomotor activity as indices of such overaction and to establish the pattern of such dysfunction.

6. **Peripheral neuropathies**. The patient with a clear-cut somatic neuropathy, especially the demyelinating neuropathies, does not require autonomic evaluation, since autonomic function is usually spared. The patient with an undiagnosed axonal neuropathy, or the patient with a suspected autonomic neuropathy, should have autonomic function tests.

7. **Syncope.** The patient with uncomplicated vasovagal syncope does not need autonomic studies. Studies are indicated in those patients in whom studies may aid in the differential diagnosis,



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patients whose recurrent syncope poses a management problem, or patients in whom a tilt study is needed to evaluate the response to treatment. In the past two decades, tilt testing has become standardized, and tilt protocols have been develop with apparent sensitivity and specificity to effectively separate normal individuals from presyncope and syncope.

8. **Monitoring the course of autonomic failure**. The twin attributes of quantitation and noninvasiveness render autonomic laboratory evaluation ideally suited to monitor the alterations of autonomic function over time.

9. **Evaluation of the response to therapy**. The autonomic deficits may lessen in response to treatment. When therapy is applied, quantitative methods are needed to evaluate if the response to therapy is adequate.

## SAFETY OF AUTONOMIC TESTS.

The noninvasive autonomic tests have an extremely high value-to-risk ratio. There are a small number of potential risks.

- The Valsalva maneuver increases intrathoracic pressure as well as intraocular and intracranial pressure. There is a small theoretical risk of intraocular hemorrhage and lens dislocation.
- Upright tilt may induce syncope, and prolonged tilt may induce cardiac arrhythmias in those so predisposed. In published reports, no complications with sequelae were reported.
- The QSART, like other tests that involve the administration of a current source, requires precautions for electrical safety. There is a small but controllable risk of local injury to the skin.
- No symptomatic arrhythmias on tilt and no intraocular complications have been encountered.
- The TST has been performed since at least 1940. In a series of 4661 sweat tests, complications were minimal.

## LIMITATIONS

Autonomic testing evaluates the physiologic responses to various stimuli. It is not a test for a specific disease; instead it investigates the degree of dysfunction of this part of the nervous system. This can aid in localization of the dysfunction, narrowing of the differential diagnosis, and in some cases making a clear diagnosis.

Autonomic testing may not be able to differentiate between similar disorders that both cause autonomic dysfunction, but can quantify the severity of autonomic dysfunction, in other cases exclude autonomic dysfunction, and thereby lead to specific recommendations for treatment.

Autonomic testing can make a diagnosis of orthostatic hypotension, delayed orthostatic hypotension, neurally mediated syncope, or postural tachycardia syndrome. However, autonomic testing cannot always differentiate between the various disorders that cause these syndromes. The role of autonomic testing in this situation is to define, clarify, and gauge the severity of the problem so that the appropriate work-up and treatment can be instituted.



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## Screening of patient before AFT :

| Autonomic Symptoms | Yes/No | Comments (Specify/Describe details, duration, frequency, situation, location etc.) |
|---|---|---|
| 1) Nasal 1.1) Dry Nose | | |
| 1.2) Running Nose | | |
| 2) Sweating Disturbances | | |
| 3) Postural Fall/ Dizziness | | |
| 4) GIT 4.1) a. Alternate D/C<br>b. Diarrhoea<br>c. Constipation<br>4.2) Discomfort/ Pain | | |
| 5) Headache Vascular:<br>(Heaviness in Head/ throbbing headache, migraine) | | |
| 6) Micturition Disturbances | | |
| 7) Occasional attack of bronchospasm:<br>(After exercise, laughter or emotion) | | |
| 8) Do you often feel too hot/ too cold:<br>(Specify) | | |
| 9) Do your extremities remain:<br>Warm/ Cold (Specify) | | |
| 10) Impotence | | |
| 11) Any stress related physical symptom:<br>(Flushing, choking, lump in throat, general weakness, tremor etc.) | | |
| 12) Medications/ Allergy to any drugs | | |

| Family History | Father/ Mother | SELF Yes/No |
|---|---|---|
| A. Alcoholism | | |
| B. Diabetes Mellitus | | |
| C. Hypertension | | |
| D. Heart Attack (CHD) | | |
| E. Obesity | | |
| F. Smoking | | |



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## The following instructions will be given to the patient before the test:

1) Please have your breakfast/lunch and report for the test after 2 hrs of food
2) Please avoid stimulants – coffee, tea, or alcohol 24 hrs before the testing.
3) Please skip any autonomic medication on the day before test
4) Fundus Evaluation in ophthalmoscopy for signs of increased IOP and HTR.
5) Drugs known to affect cardiac autonomic functions like anticholinergics (including antidepressants, antihistamines, and over-the-counter cough and cold medications), 9- α -flurocorticone, diuretics, and sympathomimetic (α and β agonist) and parasympathomimetic agents may be stopped after consultation with the physician for 2 days prior to testing.
6) Wear loose and comfortable clothing.

## The following instructions will be given to the patient at the time of the AFT test:

**For HRV Autonomic Tone:** For short-term analysis of HRV, your ECG will be recorded in the supine position for 5 min after 15 min of supine rest. Room temperature is maintained at 24°C. The subject is instructed to close their eyes and avoid the following activities during the test:

-talking
-moving hands, legs, and body
-coughing
-sleeping

**For HRV Autonomic Reactivity:** instructions will be given at the beginning of individual tests, The subject has a choice to stop the test anytime during the test if not feeling comfortable or can be stopped by a consultant if he/she feels so based on reflex response during autonomic challenge give during each reactivity test.

## Summary:

Autonomic Function Lab offers a battery of tests that evaluate basal tone and reactivity of sympathetic and parasympathetic arms. These tests can be used to screen, diagnose, and monitor autonomic symptoms in various primary as well as secondary autonomic nervous system disorders. Patients with endocrine disorders (diabetes mellitus), syncope, postural hypotension, ischemic heart diseases, gastrointestinal motility disorders, etc can benefit from AFT assessment and monitoring the response to therapy.

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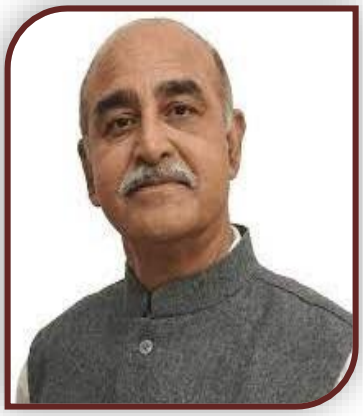

Message from the Executive Director:

I heartily congratulate the Department of Physiology for bringing this informative newsletter on "Clinical Applications of Autonomic Function Tests (AFT)". My best wishes to the entire team.

Prof. Dr. (Col) CDS Katoch, Executive Director, AIIMS, Rajkot.

## Team Physiology, AIIMS Rajkot

## Message from HOD

This is an effort to bring forward important information on Clinical Applications of Autonomic Function Tests (AFT). This initiative will be useful for Students, medical practitioners, and all readers for effective, safe, and accurate use of AFT. This e-bulletin will increase your knowledge about using AFT in clinical Physiology and Medicine.

Dr. Vivek Kumar Sharma
Professor and HOD, Department of Physiology

| | |
|---|---|
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**Quiz Time**

a) Which of the following controls visceral function?
   i) Sympathetic System
   ii) Parasympathetic System
   iii) Both
   iv) None

b) The Valsalva maneuver increases which of the following?

   i) Intrathoracic pressure
   ii) Intraocular pressure
   iii) Intracranial pressure
   iv) All of the above
   v) None of the above

c) Which of the following is not an autonomic reactivity test?

   i) Deep Breathing test
   ii) Hand Grip test
   iii) Lying to standing/Head Up Tilt
   iv) Heart Rate Variability

d) QSART test in Autonomic function testing represents?

   i) Quantitative sudomotor axon reaction test
   ii) Quantitative sudomotor axon reflex test
   iii) Quantitative sympathetic axon reflex test
   iv) Quantitative sweating axon reflex test

**Answer key: a iii, b iv, c iv, d ii**