By virtue of its many and complex functions, a complete assessment of the ANS is, of necessity, extremely complex. ANS testing has been used most often by cardiologists, gastroenterologists, urologists, and endocrinologists, with neurologists and pain specialists only recently developing ways to evaluate patients with autonomic dysfunction.

The autonomic nervous system cannot be tested directly by conventional neurophysiologic techniques, i.e., nerve conduction studies and electromyography.

The only way to assess function is indirect, by evaluating the response elicited reflexly by appropriate stimuli.

Until very recently, autonomic tests were available only in a few specialised centres.

Testing is time consuming, averaging 1 hour per patient. Furthermore, there are few skilled technicians and physicians trained in correctly interpreting the studies.

Adequate baseline acclimatisation and proper positioning of subjects are crucial.

Efforts should be made to keep the patients as comfortable as possible to limit pain-induced artefacts.

Drugs can have substantial effects on the results of ANS testing and are a common cause of abnormal results. Patients need to refrain from **caffeine, nicotine,** and **alcohol** *at least* 3 hours prior to testing.

All medications with adrenergic and anticholinergic properties need to be discontinued at least 48 hours prior to the study.

Among the drugs commonly used for treatment of pain, tricyclic antidepressants have the highest anticholinergic properties and can also impact adrenergic transmission.
SSRI antidepressants such as prozac can be continued, but mixed agents like venlafaxine and trazodone should be stopped.

Medications used to control nausea (such as chlorpromazine) have weak anticholinergic effects and may have antiadrenergic effect.

Some sedatives with antihistaminic properties (diphenydramine) may act as weak anticholinergics and should be stopped if possible.

Centrally acting agents such as **clonidine** may significantly alter the studies.
Calcium channel blockers such as verapamil can alter cardiac studies as well as studies of vaso-motor function.

Opiates (morphine and related drugs) can cause histamine release, which stimulates sweating; this can confound the test results. Sustained (slow-)- release preparations are usually not troublesome as regards testing, but short-acting ones may be.

However, discontinuing medication is likely to precipitate withdrawal, which will considerably affect test results due to precipitation of a *hyperadrenergic* state (?cold turkey': goosebumps etc.)which may include noradrenergic storm (surges of adrenaline)

Muscle relaxants usually have limited effects on autonomic testing, but ideally patients should refrain from taking them 48 hours prior to testing.

Topical capsaicin should be discontinued prior to testing because it can affect blood vessels in

the skin.

Pain medications that do not affect autonomic tests:

- NSAIDs: e.g. ibuprofen (unless tests are for orthostatic intolerance)
- Lithium
- Paracetamol
- Mexiletine
- SSRI antidepressants (fluoxetine, sertraline, fluvoxamine, citalopram);paroxetine has mild anticholinergic properties
- Anticonvulsants: carbamazepine, gabapentin
- Benzodiazepines (diazepam, clonazepam)
- Tramadol
- Muscle relaxants have generally mild anticholinergic properties; usually they do not affect significantly the studies

Table 2. Tests to assess autonomic function

Test Panel	Function Assessed
Autonomic Reflex Screen (ARS)	
Tilt table test	
Deep breathing	

Valsalva maneuver
QSART

Adrenergic vasomotor function
Cardiovagal
Cardiovagal and adrenergic vasomotor
Postganglionic cholinergic sudomotor

CRPS Screen

Temperature measurements
RSO*
QSART*
TST

Index of sympathetic vasomotor tone
Sudomotor and partially vasomotor
Postganglionic sudomotor (stimulated)
Thermoregulatory sudomotor pathways

***Performed simultaneously in bilateral, symmetrical sites.**

**(Source: Testing the Autonomic Nervous System,Paola Sandroni, MD, PhD
IASP Newsletter ,November/December 1998)**
Quantitative Sudomotor Axon Reflex Test (QSART)

After a stable baseline is obtained, 4 sites are tested simultaneously: medial distal forearm, proximal lateral leg, medial distal leg, and dorsum of the foot.

Abnormalities that can be found include: (1) reduced/absent output (2) persistent sweat activity: a sustained output after stimulus discontinuation or excessive resting sweat output indicates sweat gland overactivity.

When these abnormalities are seen in a painful neuropathy, the test is evidence of excessive sympathetic fibre activity.

Sympathetic skin response, widely used in the past, is still utilised where QSART is not available. By measuring change in skin resistance following a random electric stimulation, it provides an index of sweat production.

However, this is non-thermoregulatory sweat that occurs on the palms and soles, and is of different pharmacological and physiological properties.

Resting Sweat Output (RSO)

No stimulus is applied for this test. Simultaneous recording is performed bilaterally in standard sites (upper extremity: the medial distal forearm and hypothenar eminence; lower limb: medial distal leg above the malleolus and dorsum of the foot).

Thermoregulatory Sweat Test (TST)

This test is based on the proportional sweat production to a rise in core temperature. Temperature rise is sensed in the hypothalamus, activating the sympathetic sudomotor pathways. After appropriate acclimatisation, the subject is disrobed and dusted with alizarin red powder, which, when moist changes from orange to purple.

A thermal probe is placed in the subject's mouth (to monitor core temperature) and another one on the skin (to monitor for excessive surface heating that could cause injuries as well as induce non-thermoregulatory sweat production mediated by pain).

The subject enters a closed compartment heated by infrared heating units that control humidity and ambient temperature (respectively, 35-40% and 45-50?C). To generate the maximum sweat response, subjects are heated to a core temperature 1 degree above baseline or 38?C (whichever is greater).

If profuse sweating occurs at a lower temperature, the test is stopped. Subjects are then photographed and by computer scanning the areas of anhidrosis/hypohidrosis are mapped and expressed as percentage of body surface.

Abnormal TST results can be classified as follows:

Hypo/anhydrosis (reduced/absent sweating) can occur in different patterns:

? Distal (involving toes, legs below the knee, fingers, and in more advanced cases also the anterior lower abdomen and forehead): typically seen in peripheral neuropathies.
? Focal: follows dermatomal or peripheral nerve distribution. Also can be seen in isolated skin lesions.
? Segmental: usually larger areas than focal ones, following sympathetic distribution (such a pattern can be seen after sympathectomies).
? Regional: widespread anhydrosis but <80% body surface bordering with hypohidrosis that gradually evolves into normal areas.
? Global: diffuse, >80% anhydrosis (usually an advanced stage of the prior pattern) such as can be seen in multiple system atrophy (MSA) and progressive autonomic failure (PAF).
? Mixed: pattern not classifiable into any of the above.

Hyperhidrosis (excessive sweating) can be classified as:

? Essential (idiopathic): no known cause
? Compensatory associated with autonomic hyperreflexia.

Vasomotor Function

An autonomic screen includes 3 studies (deep breathing, Valsalva manoeuvre, tilt test), the analysis of which allows for an adequate assessment of these functions.
Blood flow has been measured with techniques such as Doppler probes.

These are very sensitive, but prone to artefact. Huge oscillations can be seen with even slight environmental stimuli, which renders the technique impractical.
Indirect assessments of vasomotor function by temperature measurement are much more popular.

Infrared thermometry and telethermography are widely used.

The most common pain indication for studies of vasomotor function is complex regional pain syndrome type I (CRPS I), or reflex sympathetic dystrophy (RSD).

Unfortunately, symptoms and signs evolve over time and can have diurnal fluctuations (vary during the day/night).

Attempts have been made to stress patients to elicit asymmetries (such as ice water immersion). These manoeuvres are time consuming and painful to the patients; a bilateral syndrome (both sides of the body) is extremely difficult to diagnose, unless florid signs are present.