

# AUTONOMIC DISORDERS



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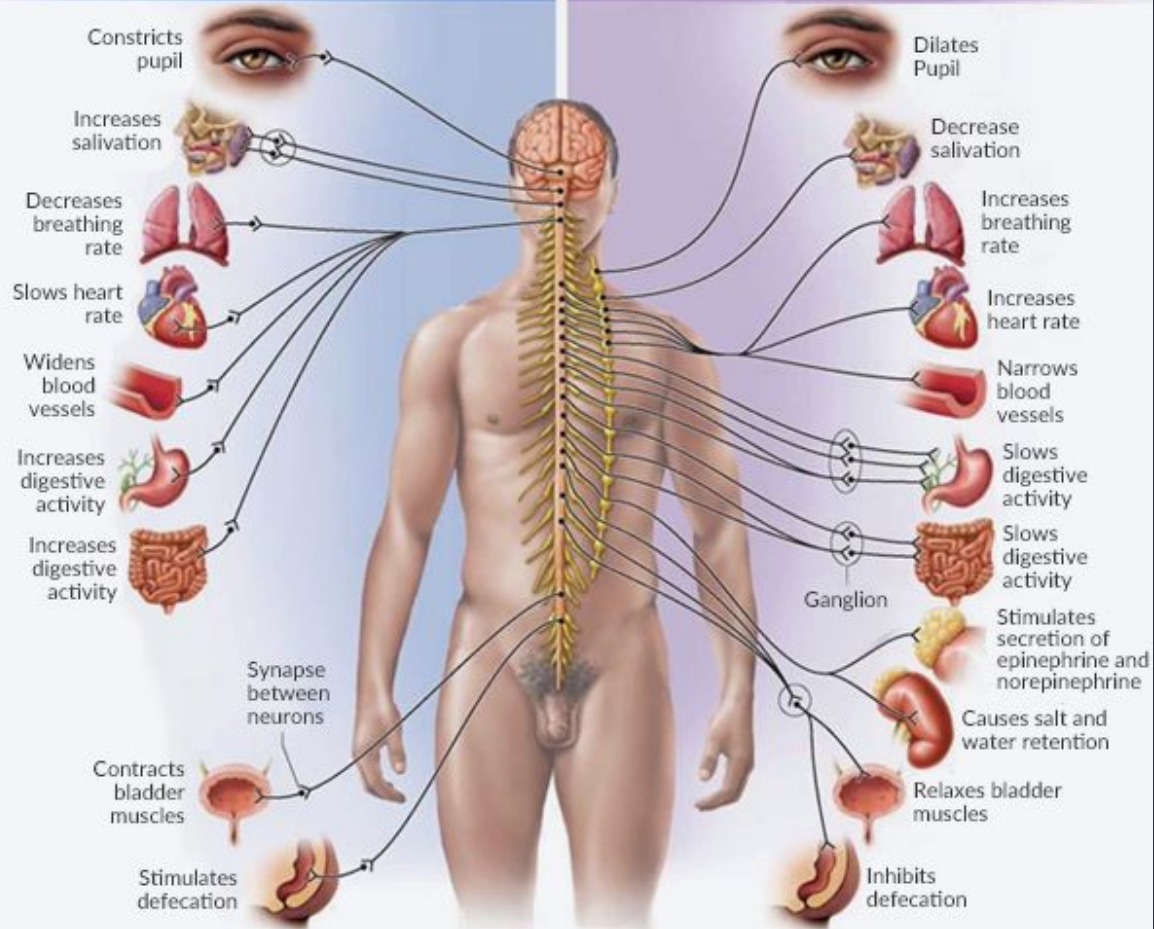
# INTRODUCTION



- The ANS regulates internal organs
- 3 main branches: SNS, PANS, and ENS
- Autonomic fibers are small and lightly myelinated to unmyelinated
- Autonomic dysfunction (dysautonomia) is a malfunction of the autonomic nerves
- Antibodies against the ganglion-type ( $\alpha_3/\beta_4$ ) nicotinic receptors  $\alpha_3$  subunit cause autoimmune autonomic ganglionopathy affecting SNS, PANS and ENS in different combinations

## Parasympathetic Nervous System

## Sympathetic Nervous System

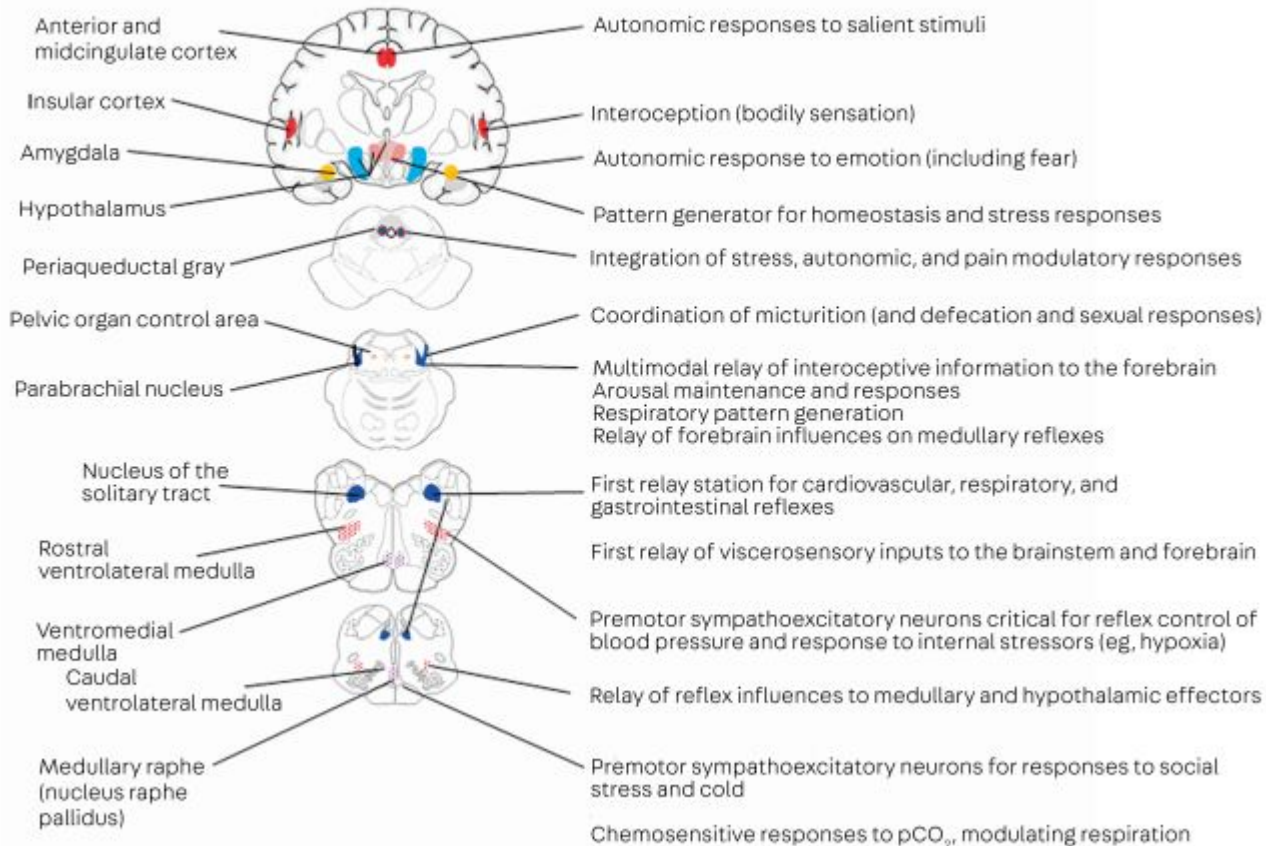


Functions of the autonomic nervous system (SANS, PANS, ENS)



## Regulatory areas

## Main functions



# CLINICAL MANIFESTATIONS



## Cardiovascular

- ▶ Postural hypotension
- ▶ Labiality of blood pressure
- ▶ Tachycardia
- ▶ Supine hypertension
- ▶ Paroxysmal hypertension
- ▶ Bradycardia

## Sudomotor

- ▶ Hypo- or anhidrosis
- ▶ Gustatory sweating
- ▶ Hypothermia
- ▶ Hyperpyrexia
- ▶ Hyperhidrosis
- ▶ Heat intolerance

## Alimentary

- ▶ Xerostomia
- ▶ Gastric stasis
- ▶ Constipation
- ▶ Dysphagia
- ▶ Dumping syndromes
- ▶ Diarrhoea

## Urinary

- ▶ Nocturia
- ▶ Urgency; retention
- ▶ Frequency
- ▶ Incontinence

## Sexual

- ▶ Erectile failure
- ▶ Retrograde ejaculation
- ▶ Ejaculatory failure
- ▶ Priapism

## Eye

- ▶ Pupillary abnormalities
- ▶ Alachryma
- ▶ Ptosis
- ▶ Abnormal lacrimation with food ingestion

# DIFFERENTIALS/MIMICKERS

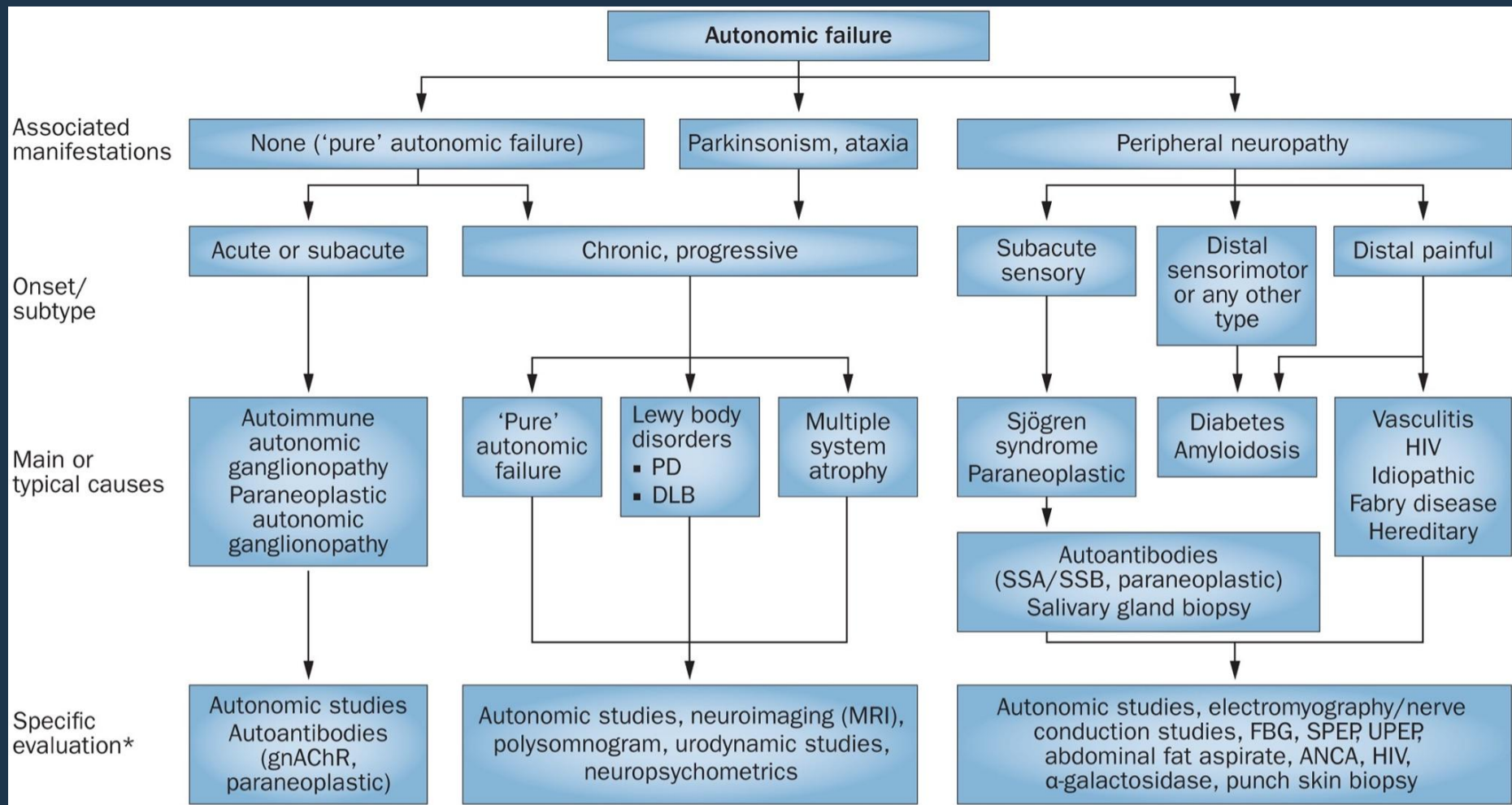


- ❖ Adrenal dysfunction
- ❖ Thyroid diseases
- ❖ Pheochromocytoma/paragangliomas
- ❖ PTSD
- ❖ Mastocytosis
- ❖ Weight loss
- ❖ Chronic volume depletion

# PATIENT APPROACH TO AUTONOMIC DYSFUNCTION



1. Identify autonomic problem
2. Identify involved systems
3. Localize process
4. **Characterize** (genetic vs acquired vs degenerative vs autoimmune)



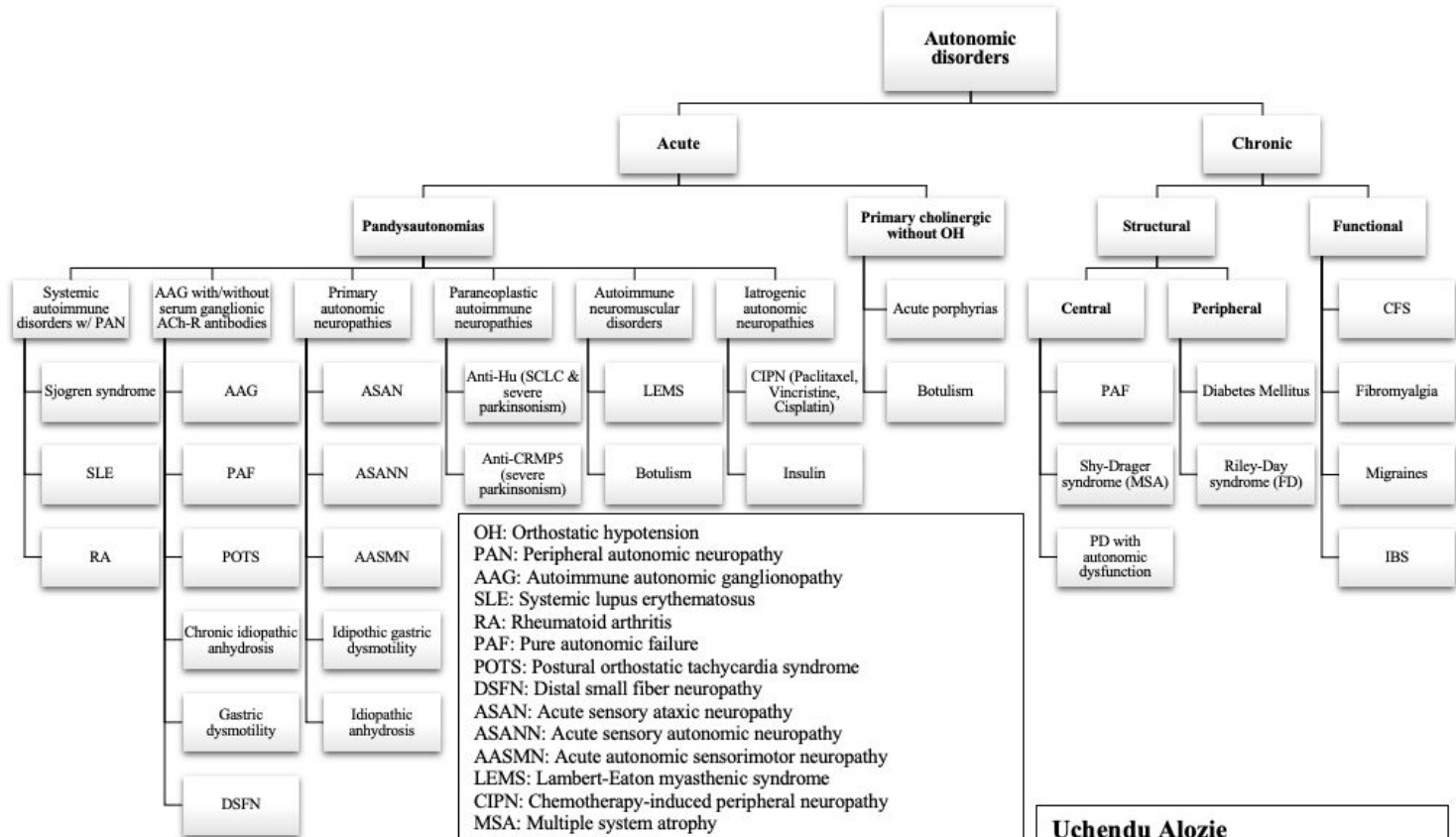
Clinical approach to autonomic failure (Benarroch, 2014)



- I. Autonomic disorders with brain involvement
    - A. Associated with multisystem degeneration
      1. Multisystem degeneration: autonomic failure clinically prominent
        - a. Multiple system atrophy (MSA)
        - b. Parkinson's disease with autonomic failure
        - c. Diffuse Lewy body disease (some cases)
      2. Multisystem degeneration: autonomic failure clinically not usually prominent
        - a. Parkinson's disease
        - b. Other extrapyramidal disorders (inherited spinocerebellar atrophies, progressive supranuclear palsy, corticobasal degeneration, Machado-Joseph disease, fragile X syndrome [FXTAS])
    - B. Unassociated with multisystem degeneration (focal CNS disorders)
      1. Disorders mainly due to cerebral cortex involvement
        - a. Frontal cortex lesions causing urinary/bowel incontinence
        - b. Partial complex seizures (temporal lobe or anterior cingulate)
        - c. Cerebral infarction of the insula
      2. Disorders of the limbic and paralimbic circuits
        - a. Shapiro's syndrome (agenesis of corpus callosum, hyperhidrosis, hypothermia)
        - b. Autonomic seizures
        - c. Limbic encephalitis
      3. Disorders of the hypothalamus
        - a. Wernicke-Korsakoff syndrome
        - b. Diencephalic syndrome
        - c. Neuroleptic malignant syndrome
        - d. Serotonin syndrome
        - e. Fatal familial insomnia
        - f. Antidiuretic hormone syndromes (diabetes insipidus, inappropriate ADH secretion)
        - g. Disturbances of temperature regulation (hyperthermia, hypothermia)
        - h. Disturbances of sexual function
        - i. Disturbances of appetite
        - j. Disturbances of BP/HR and gastric function
        - k. Horner's syndrome
      4. Disorders of the brainstem and cerebellum
        - a. Posterior fossa tumors
        - b. Syringobulbia and Arnold-Chiari malformation
  - c. Disorders of BP control (hypertension, hypotension)
  - d. Cardiac arrhythmias
  - e. Central sleep apnea
  - f. Baroreflex failure
  - g. Horner's syndrome
  - h. Vertebrobasilar and Wallenberg syndromes
  - i. Brainstem encephalitis
- II. Autonomic disorders with spinal cord involvement
  - A. Traumatic quadriplegia
  - B. Syringomyelia
  - C. Subacute combined degeneration
  - D. Multiple sclerosis and Devic's disease
  - E. Amyotrophic lateral sclerosis
  - F. Tetanus
  - G. Stiff-man syndrome
  - H. Spinal cord tumors
- III. Autonomic neuropathies
  - A. Acute/subacute autonomic neuropathies
    1. Subacute autoimmune autonomic ganglionopathy (AAG)
      - a. Subacute paraneoplastic autonomic neuropathy
      - b. Guillain-Barré syndrome
      - c. Botulism
      - d. Porphyrria
      - e. Drug-induced autonomic neuropathies-stimulants, drug withdrawal, vasoconstrictor, vasodilators, beta-receptor antagonists, beta-agonists
      - f. Toxic autonomic neuropathies
      - g. Subacute cholinergic neuropathy
  - B. Chronic peripheral autonomic neuropathies
    1. Distal small fiber neuropathy
    2. Combined sympathetic and parasympathetic failure
      - a. Amyloid
      - b. Diabetic autonomic neuropathy
      - c. Autoimmune autonomic ganglionopathy (paraneoplastic and idiopathic)
      - d. Sensory neuronopathy with autonomic failure
      - e. Familial dysautonomia (Riley-Day syndrome)
      - f. Diabetic, uremic, or nutritional deficiency
      - g. Dysautonomia of old age
    3. Disorders of reduced orthostatic intolerance-reflex syncope, POTS, associated with prolonged bed rest, associated with space flight, chronic fatigue



Low & Engstrom (2013)



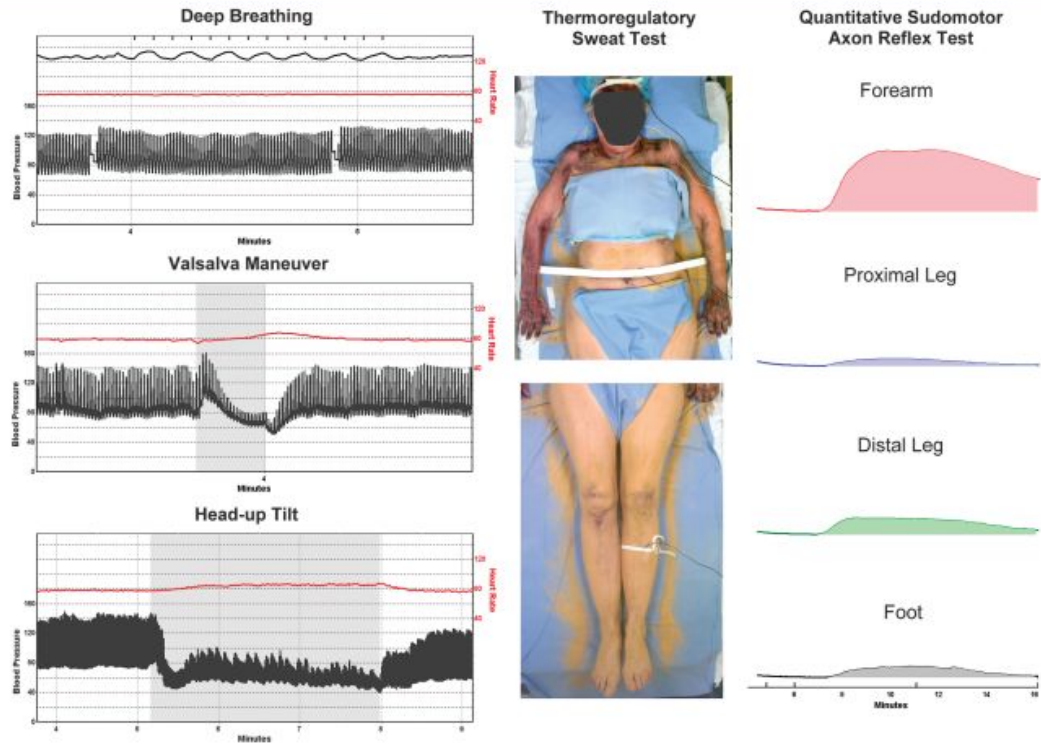
OH: Orthostatic hypotension  
 PAN: Peripheral autonomic neuropathy  
 AAG: Autoimmune autonomic ganglionopathy  
 SLE: Systemic lupus erythematosus  
 RA: Rheumatoid arthritis  
 PAF: Pure autonomic failure  
 POTS: Postural orthostatic tachycardia syndrome  
 DSFN: Distal small fiber neuropathy  
 ASAN: Acute sensory ataxic neuropathy  
 ASANN: Acute sensory autonomic neuropathy  
 AASMN: Acute autonomic sensorimotor neuropathy  
 LEMS: Lambert-Eaton myasthenic syndrome  
 CIPN: Chemotherapy-induced peripheral neuropathy  
 MSA: Multiple system atrophy  
 PD: Parkinson's disease  
 FD: Familial dysautonomia  
 CFS: Chronic fatigue syndrome  
 IBS: Irritable bowel syndrome

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# DIAGNOSIS

TEST	INTERPRETATION
<b>QSART</b>	Defines sweat loss distribution
<b>TST</b>	Provides accurate pattern of anhidrosis; can localize lesion
<b>HRV/ valsalva ratio</b>	Cardiovagal function
<b>BP response to valsalva</b>	Baroreflex function
<b>HUT</b>	Orthostatic hypotension
<b>Plasma NE supine/standing</b>	NE response to standing
<b>Cardiac MIBG</b>	Paraganglionic adrenergic denervation



**FIGURE 5-1**

Pure autonomic failure. Autonomic testing demonstrates reduced heart rate responses (red) to deep breathing and Valsalva maneuver, indicative of severe cardiovagal failure. Beat-to-beat blood pressure responses to Valsalva maneuver show adrenergic failure with absent late phase II and phase IV with prolonged blood pressure time, whereas tilt shows immediate and sustained orthostatic hypotension. The thermoregulatory sweat test demonstrates anhidrosis over the abdomen and lower extremities, and the quantitative sudomotor axon reflex test (QSART) shows reduction in sweat volumes over the lower extremity sites, indicative of postganglionic sudomotor failure.

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Coon & Singer (2020)

# MANAGEMENT



- ❖ **Treat underlying cause**
- ❖ **Avoid precipitating factors** (antihypertensives, antidepressants, levodopa, opioids, barbiturates, insulin)
- ❖ **Orthostatic hypotension**
  - **Non-pharmacological** (patient education, ↑ fluid & salt intake, counter maneuvers/postural adjustments, compressive garment, correct anemia)
  - **Pharmacological** (Midodrine, Droxidopa, Pyridostigmine, Fludrocortisone, Atomoxetine + Yohimbine?)





**THANK YOU!**



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