

Autonomic NS Disorders (SPECIFIC)

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PURE AUTONOMIC FAILURE (PAF), s. CHRONIC POSTGANGLIONIC AUTONOMIC INSUFFICIENCY, BRADBURY-EGGLESTON SYNDROME

- idiopathic, sporadic, degenerative disorder of autonomic nervous system.
- pathology - **neuron loss in autonomic ganglia**, as well as pre-ganglionic cells in medulla and spinal cord.
- begins insidiously in middle age or late adult life.
- initial complaint is often **ORTHOSTATIC HYPOTENSION** (develops gradually).
 Primary involvement of *postganglionic sympathetic neurons!*
 - low supine plasma NE levels;
 - reduced NE response to tyramine;
 - decreased neuronal uptake of NE;
 - widespread *denervation supersensitivity* - abnormally accentuated blood pressure response to intravenous norepinephrine.
- **no motor manifestations** (vs. multiple system atrophy, Parkinson's disease), no peripheral neuropathy (EMG, nerve conduction velocities, sural nerve biopsy, and CSF may be normal).
- slowly progressive, does not appear to shorten life span (prognosis better than MSA).

DOPAMINE-β-HYDROXYLASE DEFICIENCY

- hereditary disease - **inability to convert DA to NE**.
- severe orthostatic hypotension, ptosis, ejaculatory failure, nocturia, nasal congestion, hyperextensible joints.

DIAGNOSIS

- abnormal adrenergic innervation tests.
- thermoregulatory sweat test normal.
- serum NE/DA ratio is 0.1 (normal 10); decreases further with maneuvers that increase sympathetic neural discharge.

TREATMENT

- **3,4-DIHYDROXYPHENYLSERINE (DOPS)** - synthetic amino acid.
 - decarboxylated by *L-amino acid decarboxylase* to **NOREPINEPHRINE** (bypassing dopamine-β-hydroxylase step of catecholamine synthesis!).

IDIOPATHIC ORTHOSTATIC HYPOTENSION

- orthostatic hypotension of neurologic origin without evidence of other neurologic disorder.
- defect in *postganglionic sympathetic neurons* (vs. Shy-Drager syndrome - pre-ganglionic sympathetic neurons).
- no clinical involvement of CNS (vs. Shy-Drager syndrome).
- **basal plasma [NE]** is low (vs. Shy-Drager syndrome – normal).
- supine plasma [NE] *fails to rise* adequately when patient stands (as in Shy-Drager syndrome).
- *denervation supersensitivity* to IV **NOREPINEPHRINE** - abnormal rise in BP (vs. Shy-Drager syndrome - normal response).
- **TYRAMINE** (indirectly acting sympathomimetic agent that releases norepinephrine) causes blunted response (vs. Shy-Drager syndrome - normal response).
- treatment – vasoconstrictors:
 1. **MIDODRINE**
 2. **DROXIDOPA** (Northera) - FDA approved for neurogenic orthostatic hypotension (NOH) associated with Parkinson disease, multiple system atrophy, and pure autonomic failure.
 - droxidopa is converted in body to norepinephrine.
 - risk for supine hypertension

HYPOTHALAMIC SYNDROMES

Hypothalamus is most important area for integration of *behavior* with *autonomic* responses and with *neuroendocrine* control of anterior and posterior pituitary glands

1. **Neurologic defects**
 - 1) **thermoregulation** disorders (hyperthermia / hypothermia, poikilothermia)
 - *chronic* expanding lesions cause hypothermia, whereas *acute* lesions may cause hypothermia or hyperthermia.
 - 2) **emotional** disorders (rage responses)
 - 3) **arousal** disorders (hypersomnolence)
 - 4) **pyramidal / extrapyramidal** signs
 - 5) **eye** signs
 - 6) headache, vomiting, convulsions
2. **Endocrine changes** - **pituitary** dysfunction (e.g. hyper- / hypo-gonadism)

N.B. possibility of hypothalamic pathology should be kept in mind in evaluating all patients with pituitary dysfunction (esp. isolated deficiencies of single pituitary tropic hormones)
3. **Metabolic abnormalities:**
 - 1) **feeding** disorders (hyperphagia / hypophagia), obesity
 - 2) **electrolyte / osmotic** disorders (hyponatremia / hypernatremia, diabetes insipidus)

Region	Normally Regulates	Disorders
PREOPTIC	Blood volume, pressure, and electrolytes	Paroxysmal hyponatremia Essential hypernatremia
	Thermoregulation	Paroxysmal hypothermia
TUBERAL	Gastrointestinal tract and feeding	Hyperphagia (ventromedial lesions) Hypophagia (lateral lesions; must be bilateral!)
	Reproduction	Hypogonadism

Region	Normally Regulates	Disorders
	Emotions	Rage responses
POSTERIOR	Arousal	Hypersomnolence
	Descending autonomic and motor pathways	Poikilothermia

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