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)

1. **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 |
| Emotions | Rage responses |
| Posterior | Arousal | Hypersomnolence |
| Descending autonomic and motor pathways | Poikilothermia |

Bibliography for ch. “Autonomic NS disorders” → follow this [link >>](http://www.neurosurgeryresident.net/Veg.%20Vegetative%20(autonomic)%20disorders\Veg.%20Bibliography.pdf)

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