Autonomic NS Disorders (SPECIFIC)

Pure autonomic failure (PAF) and chronic postganglionic autonomic insufficiency.

**1. Dopamine-b-hydroxylation deficiency**

- 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).

**2. Dopamin-beta-hydroxylase deficiency**

- Hereditary disease - inability to convert DA to NE.
- Severe orthostatic hypotension, prostration, ejaculatory failure, nocturia, nasal congestion, hyperextensible joints.

**Diagnoses**

- Abnormal adrenergic innervation test.
- 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-dihydrosympathterol (DOPS) - Synthetic amino acid.
  - Decarboxylated by L-amino acid decarboxylase to norepinephrine (bypassing dopamine-beta-hydroxylase step of catecholamine synthesis!).

**Idiopathic orthostatic hypotension**

- Orthostatic hypotension of neurologic origin without evidence of other neurologic disorder.
  - Deficit 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 - Vasocostritors: T. saxitoxine.

**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**

Hypothalcalus is most important area for integration of behavior with autonomic responses and with neurorhondrine control of anterior and posterior pituitary glands

1. Neurologic defects
   1) Thermoregulation disorders (hyperthermia / hypothermia, poliklothermia)
   - Chronic expanding lesions cause hypothermia, whereas acute lesions may cause hyperthermia or hyperthermic.
   2) Emotional disorders (rage responses).
   3) Arousal disorders (hypercnsolence)!
   4) Gynanidal / 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 (e.g. isolated deficiencies of single pituitary tropic hormones)

3. Metabolic abnormalities:
   1) Feeding disorders (hyperphagia / hypophagia), obesity
   2) Electrolyte / somatic disorders (hyponatremia / hyponatremia, diabetes insipidus)

**Region** | Normaly Regulates | Disorders
---|---|---
Precortical | Blood volume, pressure, and electrolytes | Paroxysmal hypotension
| Thermoregulation | Essential hypotension |
| Tuberal | Gastrointestinal tract and feeding | Hyperphagia (ventromedial lesions)
| | Hypophagia (lateral lesions; must be bilateral?)
| Reproduction | Hypogonadism

**Veg3 (1)**

**Autonomic NS Disorders (SPECIFIC)**

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## Autonomic NS Disorders (Specific)

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### Bibliography for ch. “Autonomic NS disorders” ➔ follow this LINK ➔