ORTHOSTATIC HYPOTENSION (OH): CONSIDERATIONS FOR MANAGEMENT

WHAT IS THE PREVALENCE OF ORTHOSTATIC HYPOTENSION (OH)?
- The prevalence of OH varies depending on the age and comorbidities of the population. The prevalence of OH can range from ~16-20% in community residents & as high as ~50% in nursing homes, and increases exponentially with age. OH is of importance due to its association with falls, fractures, transient ischemic attacks, syncope and myocardial infarction, which all can cause serious morbidity and mortality risk.

WHAT IS ORTHOSTATIC HYPOTENSION?
- A ↓ in systolic BP ≥20mmHg or in diastolic BP ≥10 mmHg within 3 minutes of standing from sitting or supine position.
- May be asymptomatic, asymptomatic or atypical.
- Common symptoms: dizziness, light-headedness, blurred vision, fatigue, nausea, palpitations, and headache.

WHAT IS NEUROGENIC ORTHOSTATIC HYPOTENSION (nOH)?
- A failure of the sympathetic nervous system related to 1° or 2° autonomic disorders (e.g. pure autonomic failure, Parkinson’s disease, diabetic & non-diabetic autonomic neuropathies, spinal cord injury). Signs of nOH include symptoms triggered by autonomic stressors (e.g. meal, hot bath, exercise). Treatment of nOH is similar to OH.

WHAT CAUSES ORTHOSTATIC HYPOTENSION?
- OH may be multifactorial, especially in older or medically complex individuals. It may be acute/reversible, chronic/non-reversible, non-neurogenic or neurogenic. Most common causes for OH include non-neurogenic or 2° autonomic failure. (See Table 1.)

WHAT IS THE OVERALL GOAL OF OH MANAGEMENT?
- Treat if symptomatic to relieve symptoms, manage any underlying causes & improve function while ↓ risk of complications (e.g. ↓ falls). [Achieving a set BP target is not a goal. Consider life expectancy & quality of life]

Table 1: Causes of OH {may commonly be multifactorial, especially in older or if medically complex}

<table>
<thead>
<tr>
<th>4Ds: Deconditioning, Dysfunctional Heart</th>
<th>Dehydration &amp; Drugs</th>
<th>Management Overview</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute/ reversible</td>
<td>Dehydration, medications (see Table 3)</td>
<td>Deconditioning, Dysfunctional Heart</td>
</tr>
<tr>
<td>Chronic/non-reversible</td>
<td>Cardiac failure, diabetes mellitus, Parkinsonism, multiple system atrophy, trauma (blunt to chest)</td>
<td>Dehydration &amp; Drugs</td>
</tr>
<tr>
<td>Non-neurogenic OH</td>
<td>Cardiovascular: MI, aortic stenosis, constrictive pericarditis, advanced cardiac failure, hypertrophic obstructive cardiomyopathy (HOCM), arrhythmias, large varicose veins Endocrine and renal: adrenal insufficiency, diabetes insipidus, hypoaldosteronism, renal concentrating defect Venous: alcohol, postprandial dilation (spinal blood vessels), hot environment, prolonged standing Reduced intravascular volume: hemorrhage, burns, salt-losing nephropathy</td>
<td></td>
</tr>
<tr>
<td>Neurogenic OH (nOH)</td>
<td>Primary causes: pure autonomic failure, multiple system atrophy. Common causes: 2° autonomic failure (e.g. stroke, diabetes, alcoholic polyneuropathy, idiopathic parkinsonism, amyloid neuropathy, pernicious anemia)</td>
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MANAGEMENT OVERVIEW
- a) Assess Acute Medical Issues, Medications, & Hydration Status.
- b) Assess for Drug Induced Causes Of OH (see Table 3)
  - alpha-blockers e.g. terazosin; antihypertensives: e.g. diuretics (preferred alternatives: ACEI/ARB, or add or adjust dose); antiparkinsons, antipsychotics, barbiturates, ethanol, insulin, MAOIs monoamine oxidase inhibitors, nitrates, opiates, phosphodiesterase inhibitors, sedatives, TCAs (alternative: SSRIs), & trazodone
  - Consider stopping, reducing or changing the offending drug/dose
- c) NON-PHARMAOLOGICAL MANAGEMENT
  - Get Up Gradually: avoid getting up or moving too quickly (e.g. count to 15 before going from lying to sitting, & sitting to standing)
  - Stay Cool: avoid exposure to extra hot environments (e.g. hot showers).
  - Fluid (1-2.5L daily) or salt intake (up to 6-10g NaCl daily in food or as 1g tablets) unless contraindicated (e.g. heart failure, hypertremia). Drink ~500ml of water as bolus, ↑ BP in 5-30+ minutes
  - Syncope Avoidance Maneuvers: leg crossing, bending forward, squatting, toe raise, limb & abdominal contraction; give yourself a hug while standing.
  - Eat small, frequent low carbohydrate meals (e.g. small meals vs. 3 large meals) to prevent postprandial worsening of OH.
  - Caffeine intake: 1-2 cups of coffee/tea with meals if postprandial OH
- d) Consider Additional Non-drug Measures
  - Use head of the bed by 6 to 9 inches during nighttime.
  - Use abdominal binder or compressive waist-high stockings (stocking pressure ≥15-20mmHg).
  - Functional electrical stimulation in spinal cord injury
  - For men, sitting to urinate may be preferred.
  - Exercise (e.g. swimming,-recumbent bicycle or rowing).
- e) PHARMACOLOGIC MANAGEMENT OPTIONS
  - When non-pharmacological measures are inadequate, pharmacologic agents may be used in addition to nonpharmacological therapies, especially in nOH.
  - Note: [Meds treating OH can also cause supine HTN]

Table 2: Select Drugs For Treatment Of Orthostatic Hypotension

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE/ MOA/ PHARMACOKINETICS</th>
<th>ADVANTAGES/ DISADVANTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fludrocortisone FLORINEF</td>
<td>0.1mg tablets</td>
<td>0.1mg to 0.3mg daily. ↑ dose weekly or until pedal edema (if start low: 0.05mg). Maximum: 1mg/ day MOA: Synthetic mineralocorticoid (sodium &amp; water retention)</td>
</tr>
<tr>
<td>Midodrine AMATINE</td>
<td>2.5 mg, 5mg tablets</td>
<td>2.5mg to 5mg daily. Place a single dose in the morning to maximize BP response. Maximum: 5mg TID MOA: α-1-agonist</td>
</tr>
</tbody>
</table>

CONTRAINDICATIONS (C) / ADVERSE EFFECTS (AE) / DRUG INTERACTIONS (DI) / MONITOR (M)

| FLUDROCORTISONE | Dose limiting AE. K⁺ supplementation usually required. Older individuals: fluid overload |
| MIDODRINE | Can be used with fludrocortisone in refractory individuals. PRN scheduling, taken 30 to 45 minutes before upright activities. Caution elderly taking meds that ↓ HR |
| Other Considerations: | Antihypertensives should not be discontinued all at the same time in people with OH. A stepwise approach should be considered if discontinuing and tapering these medications. The risk of falls is ~2.5 times higher in the elderly with uncontrolled HTN, some relaxation of the BP goals may have to occur in order to manage the OH symptoms. Often stopping antihypertensives can treat OH in more than half of people with these symptoms. Pacemaker therapy: Atrial tachycycling option for OH and bradycardia. Dual chamber pacemakers can treat severe OH. |
**Which Medications May Worsen OH and What are the Alternatives?** 7.11,15,16,19,20

When possible, stop the medication of concern or reduce the dose of the medication before switching to another agent. Control of OH may require decrease in the intensity of BP management. **Note: Medications in Table 3 all have the potential to cause OH; some may cause or worsen OH more than others.**

<table>
<thead>
<tr>
<th>Table 3: Medications That May Worsen OH and Possible Alternatives</th>
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<tr>
<td><strong>CV</strong></td>
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<tr>
<td>β blockers (e.g. propranolol &gt; metoprolol)</td>
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<tr>
<td>α agonists (e.g. clonidine, methyldopa)</td>
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<tr>
<td>Diuretics (e.g. furosemide &gt; hydrochlorothiazide, chlorthalidone)</td>
</tr>
<tr>
<td>α blockers (e.g. doxazosin, prazosin, terazosin)</td>
</tr>
<tr>
<td>Non-DHP CCB (e.g. verapamil, diltiazem)</td>
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<tr>
<td><strong>CNS</strong></td>
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<tr>
<td>TCA’s (e.g. amitriptyline &gt; nortriptyline; clomipramine, doxepin &gt;6mg/day, imipramine, trimipramine)</td>
</tr>
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</table>

Consider a step-wise approach by tapering/discontinuing one antihypertensive at a time. If using both a BB & clonidine, taper BB first, several days before tapering clonidine to risk of rebound HTN.

**Summary: How Should Orthostatic Hypotension be Managed?** 5,7,11

A medication assessment should be done to determine if any medications may be contributory. When suitable, consider a trial of stopping or reducing medication(s) of concern or switching to another agent. **[In comorbidities such as HF, reducing doses or stopping medications could mean sacrificing life-saving effects of drugs such as ACEI & β-blockers; facilitate risk vs benefit discussions with patient/care-giver to allow for informed decisions.]** Non-pharmacological measures are important in management of OH and can be used while medications are being changed or adjusted and after the change if symptoms are still present. If OH symptoms continue to remain problematic, drug therapy may be added to non-drug measures to manage OH. **[Most OH related drug trials were studied in noH.]** Assessment of fluid status and management of dehydratio is important.

**New Drug (USA):** **Droxidopa** D−Dihydroxyphenylserine, 100, 200, 300 mg caps po TID. FDA Approval Feb/14 for Treatment of symptomatic NOH. Shown success in patients with autonomic failure and in dopamine B hydroxylase deficiency but not been studied in elderly/complex medical patients. Effectiveness beyond 2 weeks not demonstrated. **Caution:** FDA Black Box: may cause supine hypotension. AE: nausea, headache, dizziness, hypotension. (Rare: possible neuroleptic malignant syndrome, & may exacerbate heart disease.)

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**References:**

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**Pictured at left:**
1. RxFiles Drug Comparison Charts 10th Ed.
2. Geri-RxFiles – Assessing Medications in Older Adults
Additional references: