

## ORTHOSTATIC HYPOTENSION (OH): CONSIDERATIONS FOR MANAGEMENT

### WHAT IS THE PREVALENCE OF ORTHOSTATIC HYPOTENSION (OH)?<sup>1,2,3,4</sup>

- 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<sup>2,3,6,7</sup>

- A ↓ in systolic BP ≥20mmHg or in diastolic BP ≥10 mmHg within 3 minutes of standing from sitting or supine position.
- May be symptomatic, asymptomatic or atypical.
- Common symptoms:** dizziness, light-headedness, blurred vision, fatigue, nausea, palpitations, and headache.
- Less common & atypical symptoms:** syncope, dyspnea, chest pain, neck & shoulder pain. Investigate for OH with unexplained falls.

### WHAT IS NEUROGENIC ORTHOSTATIC HYPOTENSION (nOH)?<sup>8,9,10</sup>

- 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?<sup>7,11,12</sup>

- 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?<sup>1,2,3</sup>

- 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 medically complex individuals}

<b>Acute/ reversible</b>	<b>Dehydration, medications</b> (see Table 3), deconditioning, fever
<b>Chronic/non-reversible</b>	Cardiac failure, diabetes mellitus, Parkinsonism, multiple system atrophy, trauma (blunt to chest)
<b>Non-neurogenic OH</b>	<b>Cardiovascular:</b> MI, aortic stenosis, constrictive pericarditis, advanced cardiac failure, hypertrophic obstructive cardiomyopathy (HOCM), arrhythmias, large varicose veins <b>Endocrine and renal:</b> adrenal insufficiency, diabetes insipidus, hypoadosteronism, renal concentrating defect <b>Venous pooling:</b> alcohol, postprandial dilation (splanchnic blood vessels), hot environment, prolonged standing <b>Reduced intravascular volume:</b> hemorrhage, burns, salt-losing nephropathy
<b>Neurogenic OH (nOH)</b>	<b>Primary causes:</b> pure autonomic failure, multiple system atrophy. <b>Common causes:</b> 2° autonomic failure (e.g. stroke, diabetes, alcoholic polyneuropathy, idiopathic parkinsonism, amyloid neuropathy, pernicious anemia)

### MANAGEMENT OVERVIEW

#### a) Assess Acute Medical Issues, Medications, & Hydration Status.<sup>7,11,14</sup>

#### b) Assess for Drug Induced Causes Of OH (see Table 3)

- α-blockers** e.g. terazosin; **antihypertensives:** e.g. diuretics (preferred alternatives: ACEI/ARB, or adjust or split dose); **antiparkinson's**, **antipsychotics**, **barbiturates**, **ethanol**, **insulin**, **MAOIs** (monoamine oxidase inhibitors), **nitrates**, **opiates**, **phosphodiesterase inhibitors**, **sedatives**, **TCAs** (alternative: SSRI), & **trazodone**
- Consider stopping, reducing or changing the offending drug/dose

#### c) NON-PHARMACOLOGICAL MANAGEMENT<sup>2,5,7,11,13,14</sup>

- Get Up Gradually:** avoid getting up or moving too quickly (e.g. count to 15 when going from lying to sitting, & sitting to standing)
- Stay Cool:** avoid exposure to extra hot environments (e.g. hot showers).
- ↑ Fluid** (1.5-2.5L daily) or salt intake (up to 6-10g NaCl daily in food or as 1g tablets) unless contraindicated (e.g. heart failure, hypernatremia). 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. 6 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

- Raise head of the bed by 6 to 9 inches during nighttime.
- Use of abdominal binder or compressive waist-high stockings (stocking pressure ≥ 15-20mmHg).
- Exercise (e.g. swimming, recumbent bicycle or rowing).

### e) PHARMACOLOGIC MANAGEMENT OPTIONS<sup>1,2,3,5,7,10,11,12,14,15,17,19</sup>

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]**

**Fludrocortisone FLORINEF** (see Table 2) – most commonly used drug for OH.

**Midodrine AMATINE** (see Table 2) – less commonly used, but noted in literature.

**Beta blockers** (non-selective): limited role, despite negative chronotropy & inotropy.

**Caffeine:** 100-260mg TID as tablets or 1-2 cups of coffee/tea (e.g. with meals).

**Clonidine:** 0.1-0.6 mg/ day. Can ↑ venous return without significant ↑ in peripheral vascular resistance. Caution: hypotension.

**Desmopressin acetate DDAVP:** 100-800mcg po, IM 2-4mcg. Prevents nocturnal polyuria.

**Erythropoietin:** Shown to be useful in people with anemia and autonomic dysfunction.

AE: supine hypotension. Parenteral administration.

**NSAIDs:** can ↑ BP, but caution due to GI and renal adverse effects.

**Octreotide SANDOSTATIN:** Used in DM, pure autonomic failure, multiple system atrophy. More effective with midodrine than either drug if used alone. Costly; SC or IV.

**Pyridostigmine MESTINON:** 30mg BID-TID, ↑ to 60mg TID. Some success in autonomic failure. Not studied in older/complex medical patients.




**Nitroglycerin patch:** if supine HTN, nighttime dosing 8pm-8am used for nighttime congestion

**New drug on horizon:** L-Dihydroxyphenylserine DROXIDOPA, 100, 200, 300 mg FDA 2014

#### 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. While 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 tachypacing option for OH and bradycardia. Dual chamber pacemakers can treat severe OH.

**Table 2: Select Drugs For Treatment Of Orthostatic Hypertension**

DRUG	DOSE/ MOA/ PHARMACOKINETICS	ADVANTAGES/ DISADVANTAGES	CONTRAINDICATIONS (CI)/ ADVERSE EFFECTS (AE)/ DRUG INTERACTIONS (DI)/ MONITOR (M)
<b>Fludrocortisone</b> ▼ <b>FLORINEF</b> 0.1mg <sup>c</sup> tablets 	<b>Dose:</b> 0.1 to 0.3mg daily. ↑ dose weekly or until pedal edema (if start low: 0.05mg) <b>Maximum:</b> 1mg/ day <b>MOA:</b> Synthetic mineralocorticoid (sodium & water retention)	<b>Adv:</b> Considered first line therapy after failure of non-pharmacological measures <b>DI:</b> Dose limiting AE. K <sup>+</sup> supplementation usually required <b>Older individuals:</b> fluid overload	<b>CI:</b> systemic fungal infections, long term corticosteroid use, HF, renal failure <b>M:</b> fluid in & outs for adequate intake <b>AE:</b> headache, <b>supine HTN</b> , CHF, edema, ↓K <sup>+</sup> , ↑ weight <b>DI:</b> may ↓ antineoplastic (e.g. aldesleukin), BCG, corticosteroid effect, ↑ AE of natalizumab, taper off steroids prior to starting natalizumab
<b>Midodrine</b>  ▼ <b>AMATINE</b> ,g 2.5 <sup>c</sup> , 5mg <sup>c</sup> tablets 	<b>Dose:</b> 2.5mg TID, ↑ 2.5mg weekly until max dosage (for best results, AM dose given early and PM dose no later than 6pm) <b>Maximum:</b> 10mg TID <b>MOA:</b> α-1-agonist	<b>Adv:</b> Can be used with fludrocortisone in refractory individuals PRN scheduling, taken 30 to 45 minutes before upright activities <sup>2</sup> <b>DI:</b> Caution elderly taking meds that ↓ HR	<b>CI:</b> CAD, HF, acute renal failure, severe heart disease, urinary retention, thyrotoxicosis, pheochromocytoma <b>AE:</b> <b>supine HTN</b> , piloerection, pruritus, paraesthesia <b>DI:</b> ergot derivatives & MAOI may ↑ hypertensive effect, TCA may ↑ vasopressor effect, BB & CCB (non-DHP) may ↑ bradycardia, sympathomimetics may ↑ adverse/ toxic effect

If an individual cannot stop an antihypertensive, it may be replaced by agents that are less likely to cause OH. Although for some, **non-pharmacologic measures with appropriate antihypertensive medications may be sufficient.**

## WHICH MEDICATIONS MAY WORSEN OH AND WHAT ARE THE ALTERNATIVES? <sup>7,11,15,16,19,20</sup>

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 3: Medications That May Worsen OH and Possible Alternatives		
	Medications That May Worsen OH	Alternatives (less likely to cause OH)
CV	β blockers (e.g. propranolol > metoprolol)	⇒ change to an ACEI or an ARB
	α agonists (e.g. clonidine, methylodopa)	⇒ consider timing options. May split dose of antihypertensives e.g. ACEI or ARB; or nighttime dosing of at least one antihypertensive
	Diuretics (e.g. furosemide > hydrochlorothiazide, chlorthalidone)	⇒ change to tamsulosin or alfuzosin (if for BPH)
	α blockers (e.g. doxazosin, prazosin, terazosin)	⇒ DHP CCB {e.g. amlodipine, felodipine; <b>Avoid</b> nifedipine IR (Beers criteria)} ⇒ consider giving at nighttime
	Non-DHP CCB (e.g. verapamil, diltiazem)	
CNS	TCA's (e.g. amitriptyline > nortriptyline; clomipramine, doxepin >6mg/day, imipramine, trimipramine)	⇒ SSRI or SNRI (if treating depression or anxiety) or mirtazapine ⇒ If TCA indicated, may consider nortriptyline

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? <sup>5,7,11</sup>

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 dehydration is important.

**New Drug (USA): DROXIDOPA** L-Dihydroxyphenylserine, 100, 200, 300 mg; 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 hypertension**.

♣=scored 1°=primary 2°=secondary AI=active metabolite ACEI=angiotensin converting enzyme inhibitor AE=adverse effect ARB=angiotensin receptor blocker AM=morning BB=beta blocker BP=blood pressure CAD=coronary artery disease CCB=calcium channel blocker CHF=congestive heart failure CNS=central nervous system CV=cardiovascular DHP=dihydropyridine DM=diabetes mellitus e.g.=example GI=gastrointestinal HA=headache HF=heart failure HTN=hypertension hr=hour HR=heart rate HSR=hypersensitivity hx=history i.e.=that is IM=intramuscular IR=immediate release ISA=intrinsic sympathomimetic activity IV=intravenous K+=potassium LA=long acting Na+=sodium nOH=neurogenic orthostatic hypotension NT=neurotransmitter MAOI=monoamine oxidase inhibitors MI=myocardial infarction mins=minutes mg=milligrams mmHg=millimeters of mercury MOA=mechanism of action NaCl=sodium chloride OH=orthostatic hypotension PDE5 inh=phosphodiesterase type 5 inhibitors po=orally pts=patients RF=renal failure SA=short acting SBP=systolic blood pressure SC=subcutaneous sx=symptoms TCA=tricyclic antidepressant TID=three times daily vs.=versus XR=extended release

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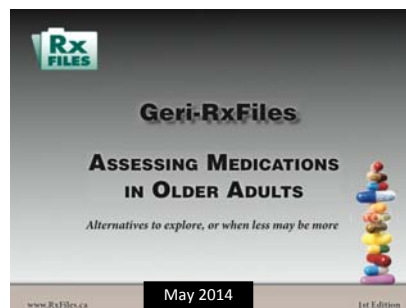
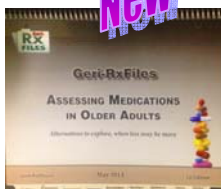
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## Possible sites of Interest:

[http://www.cdc.gov/homeandrecreationalafety/images/cdcompendium\\_030508-a.pdf](http://www.cdc.gov/homeandrecreationalafety/images/cdcompendium_030508-a.pdf)  
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