

I'M AFRAID TO FAINT AGAIN

Look carefully. This may be the face of neurogenic orthostatic hypotension (nOH).

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WHAT IS nOH?

If your patient is experiencing dizziness or any other symptom that may improve upon sitting, consider if he or she might have nOH.¹⁻⁴ nOH occurs when the autonomic nervous system fails to release appropriate amounts of norepinephrine upon standing or during postural change.³⁻⁶



This norepinephrine deficiency, often present in patients with neurodegenerative disorders, results in blood pressure fluctuations.^{3,5,6} As a result, patients may experience symptoms of nOH such as dizziness, lightheadedness, or feeling faint.^{1-3,6}

A neurologic component differentiates nOH from orthostatic hypotension

nOH is characterized by cause. While patients with nOH may experience symptoms similar to those associated with non-neurogenic orthostatic hypotension, patients with nOH have a neurologic component of the disorder unique to nOH.^{3,4,7,8}

DIFFERENTIATING FEATURES OF nOH ³		
	Non-neurogenic orthostatic hypotension	nOH
Frequency	Frequent	Less frequent
Causes	Intravascular volume loss Inadequate vasoconstriction Heart failure Physical deconditioning Medications	Failure to increase sympathetic activity and norepinephrine release upon standing
Outcome	Resolves when cause is treated	Chronic disorder
Norepinephrine increase upon standing	Normal or enhanced	Low or absent
Increase in heart rate upon standing	Pronounced	Mild or absent
Additional symptoms of autonomic failure	None	Constipation Erectile dysfunction (men) Urinary abnormalities Sweating abnormalities

Unlike blood pressure, heart rate remains fairly constant in nOH patients upon standing. If a symptomatic patient experiences an increase in heart rate less than 15 bpm within 3 minutes, he or she could have nOH. However, an increase of more than 15 bpm within 3 minutes may suggest non-neurogenic orthostatic hypotension.^{3,5,6,8,9}

Neurodegenerative disorders can cause a norepinephrine deficiency in patients

Neurodegenerative disorders, such as Parkinson's disease, can affect the neurologic functions that control the release of norepinephrine the major neurotransmitter that helps regulate blood pressure.³⁻⁷ Symptomatic episodes can occur at any point during the day when a patient's blood pressures falls below the lower limit of cerebral autoregulation, but may be worse in the morning because of nocturnal diuresis.^{1,3,5,6,10}



nOH MAY IMPACT ACTIVITIES OF DAILY LIVING

Patients with nOH may experience symptoms upon standing. These symptoms, including dizziness and lightheadedness, may range in severity and occur at any time during the day, following postural change.^{1-3,5,6,10}

A patient with nOH may be restricted due to a fear of sudden symptomatic episodes upon postural change.^{3,5}



A patient with nOH may have difficulty conducting activities of daily living without assistance.^{3,5}



A patient with nOH may lose his or her autonomy due to symptoms.^{3,5}





3 REASONS PATIENTS WITH nOH MAY GO UNDIAGNOSED:

Low awareness of nOH

nOH is considered an orphan disease, but affects many patients with Parkinson's disease, multiple system atrophy, and pure autonomic failure.^{1,3,11,12} Screening questions may help identify symptoms of nOH in these patients.^{2,8,10}

2 Mistaken nOH symptoms

In some patients, symptoms of nOH may be mistaken as symptoms of their pre-existing neurodegenerative disorder.⁵

Delayed symptomatic episodes

nOH symptoms may not present immediately following postural change. In some patients, symptomatic episodes may occur several minutes after standing.¹³ nOH may go undetected if blood pressure and heart rate monitoring are left incomplete.^{8,9} Measuring blood pressure and heart rate in both supine and standing positions may help determine if your patient has nOH.^{38,9}

WHO MAY BE AT RISK FOR nOH?

A pre-existing neurodegenerative disorder may cause nOH in patients

Many patients with Parkinson's disease, multiple system atrophy, pure autonomic failure, and autonomic neuropathies experience symptoms associated with nOH.^{1,3,11,12} Some patients may experience symptoms of nOH before their pre-existing neurodegenerative disorder becomes symptomatic.¹⁴⁻¹⁶ A patient's medical history may help determine if he or she could be at risk for nOH.^{8,9}

The following patient groups may be at risk for nOH^{1,5,8}:

- Patients with unexplained syncope
- Patients experiencing postural dizziness or nonspecific symptoms that only occur upon standing
- Patients with a pre-existing neurodegenerative disorder such as Parkinson's disease, multiple system atrophy, or pure autonomic failure
- Elderly patients



~18% of Parkinson's disease patients have symptoms of nOH¹²



81% of multiple system atrophy patients have symptoms of nOH¹²



~100% of patients with pure autonomic failure have symptoms of nOH¹¹



SYMPTOMS OF nOH OCCUR AS A RESULT OF POSTURAL CHANGES

Cardinal symptoms of nOH include dizziness and lightheadedness^{1-3,13}



The onset of symptoms occurs when a patient stands up and may disappear upon returning to a seated or supine position.^{1-3.6} In a study of nOH patients, 50% developed symptoms within a minute of standing, and 75% developed symptoms within 5 minutes of standing.¹³ Time of day, diet, and temperature may affect the severity of symptoms.^{1,3,10}

Unpredictable symptomatic episodes contribute to the vicious cycle of nOH

A patient may experience symptomatic episodes at any time during the day, specifically upon standing or during postural change.^{1-3,5,10} The unpredictability of symptoms contributes to the vicious cycle of nOH.^{1,3,5}

In this cycle, fear of symptomatic episodes contributes to increased physical inactivity. This gives way to cardiovascular deconditioning, which can, in effect, worsen nOH symptoms.^{13,5}

The vicious cycle of nOH^{1,3,5}



Screening questions may help identify nOH in symptomatic patients

Patients living with nOH may dismiss their nOH symptoms as being associated with their pre-existing neurodegenerative disorder.⁵ Screening questions may help distinguish between nOH symptoms and symptoms of a patient's pre-existing neurodegenerative disorder. Consider these screening questions^{2,8,10}:

- Do you feel dizzy or lightheaded upon standing?
- Have you fainted/blacked out recently?
- Are the symptoms worse in the morning or after meals?
- Do the above symptoms improve or disappear when you sit or lay down?

nOH DIAGNOSTIC CONSIDERATIONS

In-clinic monitoring

If a patient is experiencing symptoms associated with nOH, it may be useful to monitor his or her blood pressure and heart rate changes while standing and supine.^{3,9,17} It is important to note that symptoms may not present immediately following postural change. In some patients, symptomatic episodes may occur several minutes after standing.¹³ Recommendations from the Centers for Disease Control and Prevention include the following^{9,17}:

- 1. Have the patient lie down for at least 5 minutes
- 2. Measure the patient's blood pressure and pulse rate
- 3. Have the patient stand
- **4.** Measure the patient's blood pressure and pulse rate again after he or she has been standing for at least 1 minute and once more after 3 minutes

At-home monitoring

A physician may choose to have a patient conduct thorough at-home orthostatic measurements of blood pressure and heart rate.^{5,8,9,18} You may consider the following at-home measurement schedule:



1. First thing in the morning prior to taking any medications



2. While a patient feels symptomatic



3. At bedtime for several days (after being supine for 15 minutes)

A patient may need the assistance of a caregiver as he or she may experience symptoms while taking measurements.^{8,9}

Excluding other causes

nOH is a subset of orthostatic hypotension characterized by its neurologic component.^{3,4,8} Consider evaluating a patient's full medical history to help rule out potential causes for nOH-related symptoms, including other types of orthostatic hypotension, or medication classes that have been linked to exacerbated orthostatic hypotension.^{1,3,8,9}

For a list of medication classes known to cause nOH-like symptoms, visit nOHmattersHCP.com



Specialty testing

If a patient is experiencing symptoms associated with nOH despite taking orthostatic measurements and excluding other causes, consider the following tests^{1,3,5,8,9}:

- 24-hour ambulatory blood pressure monitoring
- Quantitative sudomotor axon reflex test
- Tilt-table test
- Thermoregulatory sweat test
- Valsalva ratio

nOH AND SUPINE HYPERTENSION

Patients with nOH may also experience supine hypertension

Up to 70% of patients with nOH also have associated supine hypertension.^{3,19} This association may be due to a patient's pre-existing neurodegenerative disorder.^{19,20} Neurodegenerative disorders can affect a patient's norepinephrine levels, the major neurotransmitter responsible for blood pressure regulation.³⁻⁷



Supine hypertension is arbitrarily defined as systolic blood pressure \geq 150 mm Hg or diastolic blood pressure \geq 90 mm Hg while in the supine position.^{5,18,20} Supine hypertension is not to be confused with essential, or primary, hypertension, which accounts for 95% of all hypertension cases. Patients with essential hypertension have, on average, higher blood pressures in both seated and standing positions. Essential hypertension is a heterogeneous disorder, with causes varying across patients.²¹

Supine and standing orthostatic measurements may reveal supine hypertension

In-clinic orthostatic measurements may be able to help identify supine hypertension in patients. Measurements taken after 5 to 10 minutes in the supine position and then repeated once a patient stands for 3 to 5 minutes may indicate that the patient has supine hypertension. Supine hypertension may persist undetected if orthostatic measurements are conducted only in the seated position.²² If the patient's blood pressure drops after standing for at least 3 minutes, he or she may also have nOH.^{3,4}

CONSIDERATIONS FOR nOH SYMPTOM MANAGEMENT

The clinical dilemma of nOH and associated supine hypertension

Many patients with nOH will also experience supine hypertension, which may confound management approaches as management of one may worsen the other.^{3,19,20,23} There are some adjustments a patient can make that may prove helpful in reducing the effects of supine hypertension, including^{3,20}:

- Avoiding lying completely flat; patients should elevate the head of their bed so that their heart is higher than their feet
- Abstaining from drinking water an hour before bed
- Refraining from any over-the-counter drugs that can worsen supine hypertension, including NSAIDs and nasal decongestants

Some medications may worsen symptoms of nOH

Some antihypertensive drugs may worsen nOH in patients. The agents found most likely to worsen nOH in patients include peripheral vasodilators such as α -receptor antagonists and nondihydropyridine calcium channel antagonists. Some agents may be less likely to exacerbate existing nOH. These include ACE inhibitors, angiotensin-receptor antagonists, and β -adrenoreceptor antagonists with intrinsic sympathomimetic activity.²²

For some patients, nOH symptoms can affect their ability to conduct activities of daily living.^{3,5,10} Management options that aim to reduce symptoms associated with nOH include adjustments that patients can implement into their daily lives.^{1,3,8,24}



Daily adjustments may help relieve symptoms of nOH in some patients

Changes in diet^{1-3,8}:

- Drinking a minimum of 2L of water daily
- Increasing salt intake
- Eating smaller meals, low in carbohydrates

Physical adjustments^{1-3,8}:

- Low-impact, lower-body strength training
- Avoiding increased core body temperature
- Elevating head of bed 6 to 9 inches
- Wearing compression stockings or abdominal binder

MATTERS neurogenic Orthostatic Hypotension

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