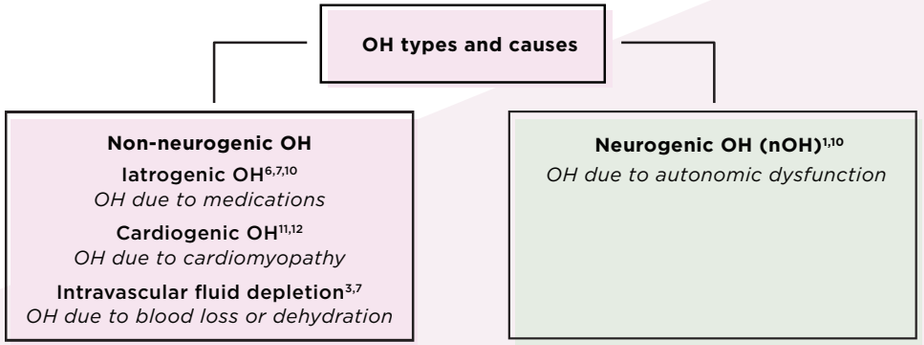

nOH
MATTERS
neurogenic Orthostatic
Hypotension
I'M AFRAID
TO FAINT AGAIN
Look carefully. This may be the face of orthostatic hypotension (OH) due to autonomic dysfunction, also known as neurogenic orthostatic hypotension (nOH).
Be sure to differentiate the various types of OH.
nOHmattersHCP.com

TYPES AND CAUSES OF OH

OH, a sustained drop of at least ≥20 mm Hg in systolic blood pressure or ≥10 mm Hg in diastolic blood pressure within 3 minutes of standing or during an upright tilt, can cause various symptoms, including dizziness and syncope.[1-3]

Approximately 12% of the elderly population within the United States has OH, but the prevalence increases with age.[4-8] OH is more common among the elderly, with 14.8% of those 65–69 years of age and 26% of those 85 and older with this condition.[9]

There can be various causes of OH. It is important to distinguish one cause from another as management may vary by type.[1,3,7]



nOH is a unique subset of OH

OH resulting from autonomic dysfunction is known as nOH.[6,10] Though the cardinal symptoms associated with nOH, such as dizziness and syncope, are similar to the symptoms of non-neurogenic OH, the neurologic component of nOH characterizes the disorder.[1,7,12]

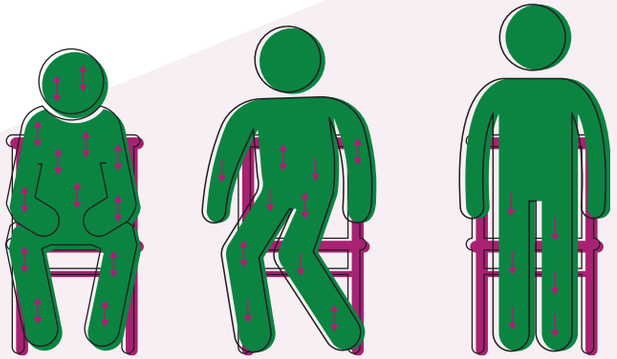
DIFFERENTIATING FEATURES OF nOH		
	nOH	**Non-neurogenic OH**
Prevalence	~1/3 of patients with OH[3,13]	~2/3 of patients with OH[3,13]
Causes	Autonomic nervous system dysfunction[1,10]	Medications[6,7,10] Intravascular volume loss[3,7] Vascular disease[11] Vasovagal syncope[1,10] Cardiomyopathy[11,12] Cardiovascular deconditioning[3,10]
Heart rate response following postural change	Inadequate compensatory increase (<15 bpm)[3,10]	Compensatory increase (>15 bpm)[10,12,14]
Associated supine hypertension	Common (up to 70%)[15]	Not present[12,16,17]
Prognosis	Chronic disorder (symptom management is the main focus)[3]	Typically resolves when underlying cause is corrected[3]

THE DISTINCT FEATURES OF nOH

OH due to autonomic dysfunction is known as nOH

In patients with nOH, the autonomic nervous system is dysfunctional. There is insufficient compensatory peripheral release of norepinephrine, the major neurotransmitter responsible for blood pressure maintenance, upon standing or following postural change.[1,10,18] Due to this norepinephrine deficiency, there is inadequate vasoconstriction to maintain blood pressure or cerebral blood flow.[3,6,18]

Hemodynamic changes in nOH patients



When a healthy individual stands, approximately 500-1000 mL of blood pools in the lower extremities and splanchnic circulation.[6,19] The resulting hemodynamic changes trigger a compensatory reflex response of the autonomic nervous system with the peripheral release of norepinephrine.[6] In patients with nOH, this response is not adequate. Furthermore, sympathetic activation is unable to affect necessary heart rate changes upon standing to make up for defective vasoconstriction.[1,7,19]

Cardinal symptoms of nOH include dizziness and lightheadedness[6,20,21]

The onset of symptoms associated with nOH may not occur immediately upon standing. In a study of 83 nOH patients, 50% developed symptoms within 1 minute of standing, and 75% developed symptoms within 5 minutes of standing.[21] Time of day, diet, hydration, and temperature may all affect the onset of symptoms in patients.[6,22,23] Additionally, symptoms of nOH have been associated with an increased risk of falling.[7,9,10,14,24]

ADDITIONAL SYMPTOMS ASSOCIATED WITH nOH[1,6,7,21]

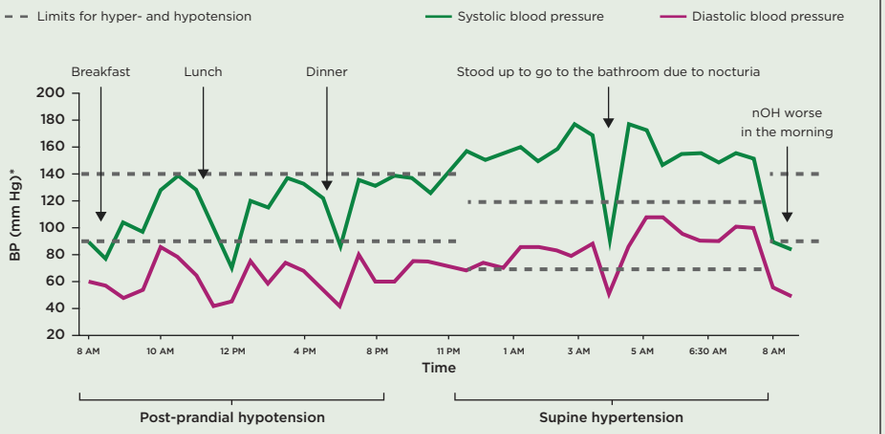
- Syncope
- Generalized weakness
- Fatigue
- Blurred vision
- Cognitive slowing
- Coat-hanger (neck and shoulder) pain
- Orthostatic dyspnea
- Orthostatic angina

SYMPTOMS CAN MANIFEST AFTER A PATIENT WITH nOH STANDS UP AND IMPROVE WHEN A PATIENT SITS DOWN.[3,20]

nOH SYMPTOMS MAY AFFECT A PATIENT'S DAILY ACTIVITIES

Cardinal nOH symptoms can occur when a patient's blood pressure falls below the lower limit of cerebral autoregulation.[3,22] Symptomatic episodes can occur at any time of the day and may vary from day to day. Patients may feel symptomatic within 30 minutes of eating a meal because of associated postprandial splanchnic vasodilation.[3,10,22,23] The morning may be especially problematic for patients due to nocturnal diuresis.[6,22] At night, healthy individuals experience a decrease or dip in blood pressure. However, in patients with nOH, blood pressure may spike into the hypertensive range while supine. This transient increase in blood pressure is known as reverse dipping.[25,26] The variability of symptoms may make certain daily activities challenging.[10,22,23]

BP variances throughout the day can result in unpredictable symptomatic episodes[10,22,23,27]



Graphic adapted from: Kaufmann H, Palma JA. *Clin Auton Res*. 2017;27:39-43.

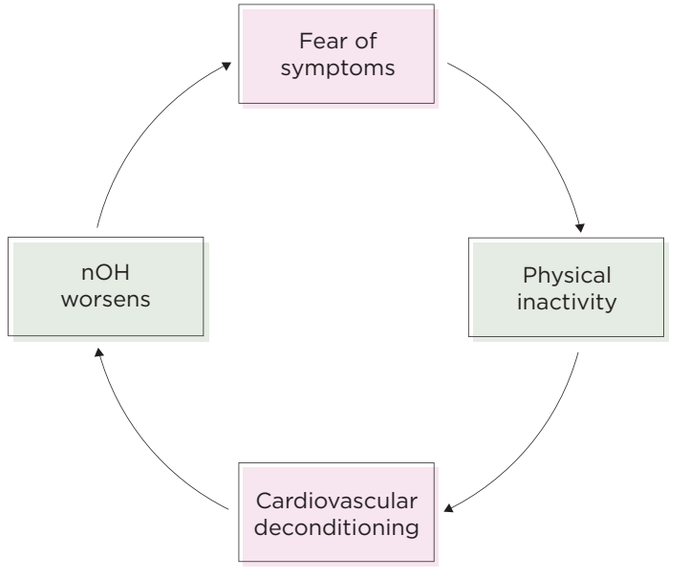
*Represents a 24-hour ambulatory BP recording and is for demonstrative purposes only.

Unpredictable symptomatic episodes contribute to the vicious cycle of nOH

Symptomatic episodes can be unpredictable with respect to frequency and severity of events.[3,6,10,22,23] This unpredictability of events contributes to a vicious cycle of nOH.[3,6,10]

In this cycle, fear of symptomatic events may lead patients to reduce physical activity, which can lead to cardiovascular deconditioning and the exacerbation of nOH symptoms.[3,6,10]

The vicious cycle of nOH[3,6,10]



Symptoms of nOH may negatively affect a patient

A patient with nOH may[10]:

- Feel restricted due to a fear of sudden symptomatic episodes upon postural change
- Have difficulty conducting daily activities without assistance
- Have less autonomy due to symptoms

DIAGNOSTIC CONSIDERATIONS

nOH, a subset of OH, is characterized by autonomic dysfunction. When diagnosing a symptomatic patient, excluding other causes of OH may be helpful.[1,3,12,14]

Consider these questions when evaluating medical history[6,7,12,13]:

- Does your patient have syncope or falls of unknown causes?
- Does your patient have a neurological disorder associated with autonomic dysfunction, such as Parkinson's disease?
- Is your patient elderly?
- Is your patient taking medications that can exacerbate OH?

Excluding other causes

Many factors have been identified to cause OH.[1,6,7,10-12]

Non-neurogenic OH

Iatrogenic OH

Causes include use of[6,7,10]:

- Vasodilators
- Antihypertensives
- Tricyclic antidepressents

Cardiogenic OH

Causes include[11,12]:

- Hypovolemia
- Cardiac insufficiency
- Vascular disease

Intravascular fluid depletion

Causes include[3,7]:

- Blood loss
- Dehydration

Neurogenic OH (nOH)

Cause is inadequate vasoconstriction, often as a result of[1,10]:

- Autonomic neuropathy
- Parkinson's disease
- Multiple system atrophy
- Pure autonomic failure
- Dopamine beta-hydroxylase deficiency

In-clinic orthostatic measurements

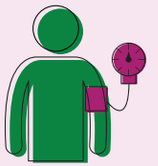
If a patient is experiencing symptoms associated with nOH, it may be useful to monitor his or her blood pressure and heart rate changes while standing and supine.[3,14,28] Symptoms may not present immediately following postural change but may occur several minutes after standing.[21] If a patient is unable to stand long enough to conduct accurate measurements, a tilt-table test may aid in diagnosing nOH.[3,10,14]

Recommendations from the Centers for Disease Control and Prevention include the following[28]:

1. Have the patient lie down for 5 minutes.

2. Measure the patient's blood pressure and pulse rate.

3. Have the patient stand.



4. Repeat blood pressure and pulse rate measurements at 1 and 3 minutes after standing.

MANAGEMENT CONSIDERATIONS

The goal of management should be to reduce symptoms in patients with nOH[6,12,29]

Due to the high degree of hemodynamic variability in nOH patients, restoring normal blood pressure may not be a realistic management goal.[6,12,29] Understanding the underlying cause for a patient's symptoms can point to the diagnosis, and a path for symptom management may be possible.[10]

Daily adjustments that may help relieve symptoms of nOH in some patients

For some patients, nOH symptoms can affect their ability to conduct daily activities.[10] Management options that aim to reduce symptoms associated with nOH include the following[3,6,12,29]:

Changes in diet[3,6,12]:

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

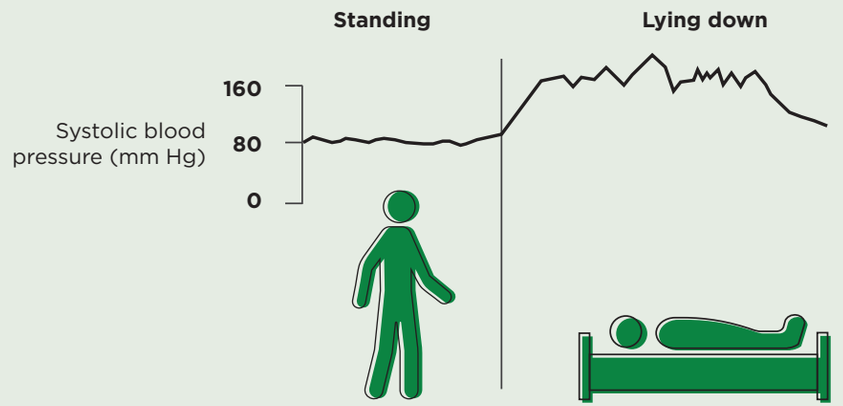
Physical adjustments[3,6,12]:

- Elevating head of bed 6 to 9 inches
- Exercising in the recumbent position (eg, stationary bicycle, rowing machine)
- Avoiding increased core body temperature
- Wearing compression stockings or abdominal binder

Up to 70% of patients with nOH also have associated supine hypertension[15]

Patients with autonomic failure may lack the normal blood pressure buffering mechanisms that offset both hypo- and hypertension.[12,17,22] Supine hypertension has been defined as systolic blood pressure ≥150 mm Hg and/or diastolic blood pressure ≥90 mm Hg while supine.[10,16,25] Supine hypertension is not to be confused with essential or primary hypertension. Patients with essential hypertension have high blood pressures in seated and standing positions.[17,30]

Patients with supine hypertension experience elevated systolic blood pressure while recumbent*[16,25]



*Blood pressure trace is not from an actual patient and is for demonstrative purposes only.

The high prevalence of supine hypertension in patients with nOH may confound management approaches as management of supine hypertension may worsen nOH symptoms.[3,15,16,31] There are some adjustments a patient can make that may prove helpful in reducing the effects of supine hypertension, including[3,16]:

- Avoid lying completely flat; elevating the head of their bed 6 to 9 inches so that their heart is higher than their feet
- Abstaining from drinking water an hour before bed
- Refraining from any drugs that can worsen supine hypertension, including NSAIDs and nasal decongestants

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