EXPERTOPINION

By Randolph W. Evans, MD

# Unilateral Paresthesias Due to Hyperventilation Syndrome

## This common condition responds remarkably well to treatment, but the wide array of potential symptoms makes it difficult to discern its origins.

**CASE**: *A 53-year-old male was referred by his cardiologist with a two-month history of dizzy spells occurring about four times per week lasting one to two minutes. He reported a sensation of lightheadedness associated with tingling of the left ankle. There was no associated spinning, hearing loss, tinnitus, paresis, ataxia, diplopia, chest pain, shortness of breath, alteration of consciousness or headache. The episodes occurred while lying, sitting or with activity.*

*There was a history of hypertension and hyperlipidemia but no diabetes or ischemic heart disease. He had a documented Mobitz type I and third degree AV block. On a recent heart monitor, there was no correlation between heart block and the episodes. A stress echocardiogram was normal.*

*He has occasional headaches, described as a bifrontal aching with a 5/10 intensity without associated symptoms relieved by ibuprofen within a few hours. Past medical history was otherwise negative. In addition to ibuprofen, medications included Lipitor, Norvasc and Atacand.*

*General physical and neurological exams were normal. The carotid pulses were symmetric without bruits. A Dix-Hallpike maneuver was negative.*

*The patient was asked to hyperventilate. This exactly reproduced his complaints of dizziness and tingling of the left ankle.*

*Question: What is the cause of the episodes?*

### Expert Opinion

The history and reproduction of symptoms with the hyperventilation provocation test is consistent with hyperventilation syndrome,[6] which can be a diagnosis of exclusion. TIAs and partial seizures are possible but quite unlikely.

I discussed with the patient the likely diagnosis and treatment with breathing into a paper bag held over the mouth and nose for 1-2 minutes during an attack. An MRI of the brain and neck was normal, as was an EEG. On follow-up four months later, he reported two more episodes in the first two weeks aborted by breathing into a paper bag and then no further episodes.

According to one consensus definition, "hyperventilation syndrome is a syndrome characterized by a variety of somatic symptoms induced by physiologically inappropriate hyperventilation and usually reproduced in whole or in part by voluntary hyperventilation."[7] Acute hyperventilation with obvious tachypnea accounts for about one percent of all cases. The other 99 percent are due to chronic hyperventilation in which there may be a modest increase in respiratory rate or tidal volume that may not even be apparent to the patient or a medical observer.

Hyperventilation syndrome occurs in about six to 11 percent of the general population.[8] Most studies have reported hyperventilation syndrome occurring two to seven times more frequently in women than in men, with most patients ranging in age between 15 and 55 years. The prevalence of chronic hyperventilation is highest in middle-aged women.

### Clinical Manifestations

The manifestations of hyperventilation syndrome are listed in Table 1. Patients with different symptoms may see different specialists. Cardiologists may see those with complaints of chest pain, palpitations and shortness of breath. Neurologists frequently see patients describing dizziness and paresthesias.

The most common cause of distal symmetrical paresthesias is hyperventilation syndrome.[9] Although physicians generally recognize it as the source of bilateral paresthesias of the face, hands and feet, many neurologists are not aware that hyperventilation can cause unilateral paresthesias, as in this case.

In two studies of volunteer groups, hyperventilation produced predominantly unilateral paresthesias in 16 percent of subjects, and these involved the left side in over 60 percent.[10,11] In the volunteer group of 145 medical students, unusual patterns of

### Origins of Hyperventilation Syndrome

The symptoms of hyperventilation syndrome have been recognized for over 140 years. DaCosta described Union soldiers during the Civil War with mysterious symptoms he called *irritable heart*.[1] Gowers used the terms *vagal* and *vaso-vagal* in 1907 for similar symptoms.[2] During World War I, Lewis reported symptoms often associated with fatigue as *soldier's heart*.[3] In 1922, Goldman made the connection between forced ventilation and tetany.[4] Finally, in 1937, Kerr, Dalton and Gliebe coined the term *hyperventilation syndrome*, noting, "Patients presenting the well-known pattern of symptoms haunt the offices of physicians and specialists in every field of medical practice. They are often shunted from one physician to another, and the sins of commission inflicted upon them fill many black pages in our book of achievement."[5]

numbness included the following: the shoulders; one side of the forehead; one side of the abdomen; one foot; and both hands as well as the right toes.[11] Of those with hand numbness, often only the fourth and fifth fingers are involved. One student reported numbness of the hands and tunnel vision and another reported numbness of the left hand and diplopia.

Unilateral paresthesias more often involving the left side have also been reported in patients with hyperventilation syndrome.[10,12-15] Of 78 patients presenting to a neurology outpatient clinic with symptoms of hyperventilation, 36 percent reported paresthesias.[13] Distribution was as follows: upper limbs in 89 percent of cases; lower limbs 36 percent; face 29 percent; trunk 18 percent. The paresthesias were unilateral in 10 percent of cases. Patients often reported paresthesias with more than one distribution.

Patients may report a variety of psychological complaints, commonly including anxiety, nervousness, unreality, disorientation or feeling "spacey." Impairment of concentration and memory may be described as part of episodes or alternatively as symptoms of an underlying anxiety disorder or depression. A patient's concern about the cause may result in feelings of impending death, fear or panic, which may accentuate the hyperventilation. Patients with hyperventilation syndrome have a mean group profile very similar to patients with pseudoseizures: a neurotic pattern where patients respond to psychological stress with somatic symptoms. Other complaints such as déjà vu or auditory and visual hallucinations are rare.[11]

## Etiology and Pathophysiology

Hyperventilation syndrome is frequently associated with anxiety or stress, although some patients have no detectable psychiatric disorder and develop a habit of inappropriately increased ventilatory rate or depth.[16] Common triggers of acute hyperventilation syndrome include anxiety, nausea and vomiting, and fever due to the common cold.

Acute hyperventilation reduces arterial $pCO_2$, resulting in alkalosis. Respiratory alkalosis produces the Bohr effect, a left shift of the oxygen dissociation curve with increased binding of oxygen to hemoglobin and reduced oxygen delivery to the tissues. The alkalosis also causes a reduction in plasma $Ca^{2+}$ concentration. Hypophosphatemia may be due to intracellular shifts of phosphorus caused by altered glucose metabolism. In chronic hyperventilation, bicarbonate and potassium levels may decrease because of increased renal excretion. Finally, stress can produce a hyperadrenergic state that may trigger hyperventilation through beta-adrenergic stimulation.[17]

Central and peripheral mechanisms have been postulated for production of neurologic symptoms during hyperventilation.[18] Voluntary hyperventilation can reduce cerebral blood flow by 30 to 40 percent. Symptoms and signs such as headache, visual disturbance, dizziness, tinnitus, ataxia, syncope and various psychological symptoms may be produced by diminished cerebral perfusion.

The precise cause of generalized slowing of brain waves during hyperventilation is not certain. This response is most common and pronounced in children and teenagers, diminishes in young adults, and is rare in old persons. A brainstem-mediated response to hypocarbia has been proposed. The response may be due to metabolic rather than just hemodynamic factors. Hypoglycemia can accentuate the generalized slowing or buildup.

There have been additional postulates to explain the manifestations of hyperventilation. Muscle spasms and tetany may be due to respiratory alkalosis and hypocalcemia. The finding that there is no relationship between the

**Table 1. Symptoms and Signs of Hyperventilation Syndrome**

**General**
- Fatigue, exhaustion, weakness, sleep disturbance, nausea, sweating

**Cardiovascular**
- Chest pain, palpitations, tachycardia, Raynaud phenomenon

**Gastrointestinal**
- Aerophagia, dry mouth, pressure in throat, dysphagia, globus hystericus
- Epigastric fullness or pain, belching, flatulence

**Psychological**
- Impaired concentration & memory
- Feelings of unreality, disorientation, confused/dream-like feeling, déjà vu
- Hallucinations
- Anxiety, apprehension, nervousness, tension, fits of crying, agoraphobia
- Neuroses, phobias, panic attacks

**Neurologic**
- Headache, pressure in the head, fullness in the head, head warmth
- Blurred vision, tunnel vision, momentary flashing lights, diplopia
- Dizziness, faintness, vertigo, giddiness, unsteadiness
- Tinnitus
- Numbness, tingling, coldness of face, extremities, trunk
- Muscle spasms, muscle stiffness, arpopedal spasm, generalized tetany, tremor
- Ataxia, weakness
- Syncope, seizures

**Respiratory**
- Shortness of breath, suffocating feeling, smothering spell, inability to get a good breath or breathe deeply enough, frequent sighing, yawning

rate of fall of $pCO_2$ and the onset of dizziness and paresthesias suggests that symptoms may be due to hypophosphatemia.[19] Hypophosphatemia can result in symptoms such as fatigue, dizziness, poor concentration, disorientation and paresthesias. A hyperadrenergic state may result in tremor, tachycardia, anxiety and sweating. Hypokalemia can cause muscle weakness and lethargy.

The cause of bilateral and unilateral paresthesias is not certain; evidence exists for both a central and peripheral mechanism. A reduction in the concentration of extracellular $Ca^{2+}$ may increase peripheral nerve axonal excitability, resulting in spontaneous bursting activity of cutaneous axons, perceived as paresthesias.[9] Lateralization of symptoms might be explained by anatomic differences in the peripheral nerves and their nutrient vessels.[20]

Alternatively, symmetrically decreased cerebral perfusion could account for bilateral paresthesias and asymmetrically decreased perfusion for unilateral paresthesias. O'Sullivan and colleagues reported nonspecific, asymmetric slowing of brain waves in the hemisphere opposite to the side of unilateral paresthesias in hyperventilators and normal bilateral somatosensory evoked potentials.[15] Although anatomic differences in the cerebral vasculature might explain the unilateral paresthesias, normal magnetic resonance angiographic findings in two cases argue against this.[11] Also, there is a single report of asymmetrically decreased cerebral blood flow with decreased flow in the right parietal area with left-sided symptoms.[11]

Why unilateral paresthesias occur more often on the left side of the face and body is unknown. One hypothesis is that psychosomatic symptoms are associated with right hemisphere psychological processes; during stress and emotional arousal, the right hemisphere is activated more than the left. Symptoms of conversion or hyperventilation are more likely to occur on the left side of the face and body.[10,15] However, this does not explain the increased frequency of left-sided paresthesias in normal subjects who are asked to hyperventilate.

## Diagnostic Evaluation

The acute form of hyperventilation syndrome is easily recognized. However, the chronic form is less easily recognized because the breathing rate is not reported as rapid or does not appear rapid and because the symptoms may appear to be atypical. For example, a respiration rate of 18 per minute combined with an increased tidal volume of 750ml per minute may lead to overbreathing that is not easily detectable. Since the chronic disorder is intermittent, spot arterial $pCO_2$ or end tidal volume $pCO_2$ results can be normal. The diagnosis depends on reproducing some or all of the symptoms with the hyperventilation provocation test and excluding other possible causes by either clinical reasoning or laboratory testing when indicated. Patients frequently report only one or two symptoms but, on performing the hyper-

ventilation provocation test, report other symptoms that appear during their typical episodes but that they had forgotten.

The hyperventilation provocation test can be performed with either an increased ventilation rate of up to 60 per minute or simply deep breathing for three minutes.[21] Based on a study of healthy subjects, a minimum duration of three minutes and end-tidal $pCO_2$ decreasing to at least 1.9 kPa or dropping well over 50 percent of baseline should elicit symptoms.[22] Dizziness, unsteadiness and blurred vision commonly develop within 20 to 30 seconds, especially with the patient in the standing position; paresthesias start later.[21]

Chest pain is reported by 50 percent of patients after three minutes of hyperventilation and by all by 20 minutes. For clinical purposes, measurement of end tidal volume $pCO_2$ is not necessary. In addition, there is no clear correlation between $paCO_2$ and neurologic signs.[23] The hyperventilation provocation test should be avoided or performed with caution in patients with ischemic heart disease, cerebrovascular disease, pulmonary insufficiency, hyperviscosity states, significant anemia, sickle cell disease or uncontrolled hypertension.[8]

For some patients, symptoms cannot be reliably reproduced during the hyperventilation provocation test or even on consecutive tests.[24] In some cases, the hyperventilation provocation test lacks test-retest reliability. For others, antecedent anxiety and stress, not present during the test, may predispose to symptom formation, perhaps because of a hyperadrenergic state.[13,17] Different patterns of hyperventilation with different respiratory rates, tidal volumes and durations may induce different symptoms.[24] Finally, as a response to a change in body position from supine to standing, patients with hyperventilation syndrome have an accentuated increase in ventilation that can be calculated with noninvasive measurements of pulmonary gas exchange, and that distinguishes them from healthy subjects.[25]

From my experience with patients with predominantly neurologic complaints, the concept of hyperventilation syndrome is valuable and the hyperventilation provocation test, despite its recognized shortcomings, is useful. In the individual case, if the provocation test fails to reproduce the symptoms but clinical suspicion persists and other conditions have been excluded, treatment such as breath holding, slow breathing or breathing into a paper bag can certainly be suggested on a trial basis.

## Prognosis

In a follow-up study of children and adolescents, 40 percent were still hyperventilating as adults and many suffered from chronic anxiety.[26] One half of patients with acute hyperventilation recover without treatment.[24] In 10 percent of those with chronic hyperventilation, symptoms may persist for more than three years.[24] With proper management, perhaps 70 to 90 percent of adults become symptom-free.

## Management

Treatments that have been proposed include patient reassurance and education, instructions to hold the breath, breathe more slowly, or breathe into a paper bag, along with breathing exercises and diaphragmatic retraining, biofeedback, hypnosis, psychological and psychiatric treatment, and medications such as beta blockers, benzodiazepines, and antidepressants.[18] A study of nonpharmacologic treatments found efficacy for educational sessions, breathing techniques and retraining, and progressive relaxation; the greatest improvement occurred in the group given an explanation and eight sessions of breathing retraining.[27] There is a lack of well-controlled treatment trials comparing these approaches.

In my experience, most patients respond to reassurance, education and instructions to hold the breath, breathe more slowly, or breathe into a paper bag. Providing written materials such as Lance's handout[28] may be worthwhile. If significant symptoms of stress, anxiety or depression are present, appropriate medication and psychological or psychiatric referral may be helpful. **PN**

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