

Hyperventilation syndrome from MedLink Neurology available at www.medlink.com

Contributors

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Synonyms

Hyperventilation; Neurocirculatory asthenia; Soldier's heart; Soldier heart

Historical note and nomenclature

According to 1 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" ([Lewis and Howell 1986](#)). Acute hyperventilation with obvious tachypnea accounts for about 1% of all cases of hyperventilation ([Lum 1975](#)). The other 99% of cases are due to chronic hyperventilation where there may be a modest increase in respiratory rate or tidal volume, which may not even be apparent to the patient or a medical observer.

The symptoms of hyperventilation syndrome have been recognized for at least 125 years. In 1871, Da Costa published a paper, *On Irritable Heart; a Clinical Study of a Form of Functional Cardiac Disorder and its Consequences*, describing 300 Union soldiers in the American Civil War with a mysterious illness ([Da Costa 1871](#)). He felt the condition could be seen in private practice as well. Symptoms included palpitations, chest pain, shortness of breath or oppression on exertion, indigestion, abdominal distention, and diarrhea. Headache, giddiness, disturbed sleep, and **dizziness** were "all indicative of disturbed circulation in the cerebro-spinal centres." Da Costa reasoned that "the heart has become irritable, from its over-action and frequent excitement..." During World War I, similar symptoms often associated with fatigue were also attributed to cardiovascular dysfunction and described as "soldier's heart" ([Lewis 1919](#)) or "neurocirculatory asthenia" ([Levine 1965](#)). In contrast, Gowers used the terms "vagal" and "vaso-vagal" for these symptoms, which could include numbness and tingling of the extremities ([Gowers 1907](#)).

In 1922, Goldman was the first to make the connection between "forced ventilation" and tetany and postulated that the tetany was due to alkalosis ([Goldman 1922](#)). Kerr and colleagues introduced the term "hyperventilation syndrome," and they described the variety of symptom complexes caused by physical phenomena associated with anxiety states, which could often be reproduced in the examining room with the "hyperventilation test" ([Kerr et al 1937; 1938](#)).

Lewis contended that acute and chronic hyperventilation syndrome occurred frequently and described the common and atypical presentations, pathophysiology, and therapy ([Lewis 1953](#)). He reported that **paresthesias** were occasionally asymmetrical and could even be unilateral. Tavel described patients with hyperventilation syndrome presenting with unilateral paresthesias at times associated with subjective unilateral weakness that involved the left side of the face and body more commonly than the right ([Tavel 1964](#)).

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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 (Pincus 1978; Perkin and Joseph 1986).

Table 1. Symptoms and Signs of Hyperventilation Syndrome

General

- Fatigability, 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

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, carpedal spasm, generalized tetany, tremor
- Ataxia, weakness
- Syncope, seizures

Psychological

- Impairment of concentration and memory
- Feelings of unreality, disorientation, confused or dream-like feeling, déjà vu
- Hallucinations
- Anxiety, apprehension, nervousness, tension, fits of crying, agoraphobia
- Neuroses, phobias, panic attacks

Respiratory

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

The most common cause of distal symmetrical **paresthesias** is hyperventilation syndrome (Macefield and Burke 1991). Although physicians generally recognize bilateral paresthesias of the face, hands, and feet as due to hyperventilation syndrome, many neurologists are not aware that hyperventilation can cause unilateral paresthesias. In 2 studies of volunteer groups, hyperventilation produced predominantly unilateral paresthesias in 16%, and these involved the left side in over 60% (Tavel 1964; Evans 1995; 2005). Of those with hand numbness, often only the fourth and fifth fingers are involved. Unusual patterns of numbness reported include 1 side of the forehead, the shoulders, and 1 side of the abdomen. Unilateral paresthesias more often involving the left side have also been reported (Tavel 1964; Blau et al 1983; Perkin and Joseph 1986; Brodtkorb et al 1990; O'Sullivan et al 1992).

Patients may report a variety of psychological complaints, commonly including anxiety, nervousness, unreality, disorientation, or feeling "spacy." Impairment of concentration and memory may be described as part of episodes or alternatively as symptoms of an

underlying anxiety neurosis or depression. A patient's concern about the cause of the various symptoms of hyperventilation 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 (Brodtkorb et al 1990). Other complaints such as déjà vu or auditory and visual hallucinations are rare (Allen and Agus 1968; Evans 1995; 2005).

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Clinical vignette

A 47-year-old woman presented with a few-week history of daily episodes of lightheadedness, nervousness, and feelings of weakness, coupled with numbness of the left arm, left leg, and perioral area. The numbness was associated with chest tightness and difficulty inhaling and lasted minutes at a time. She denied any recent stress or depression. She had normal blood and treadmill tests. Past medical history was unremarkable. General physical and neurologic examinations were normal. The hyperventilation test resulted in numbness and tingling periorally, as well as in the left upper and lower extremities. These symptoms were associated with chest tightness. A MRI scan of the brain with MRA was normal. She was advised to slow her breathing or breathe into a paper bag if additional spells occurred. On followup, the episodes had resolved.

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Etiology

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 (Bass and Gardner 1985).

Common triggers of acute hyperventilation syndrome include anxiety, **nausea and vomiting**, and fever due to the common cold (Hirokawa et al 1995).

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Pathogenesis and pathophysiology

Acute hyperventilation reduces arterial $p\text{CO}_2$, 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 (Brautbar et al 1980). In chronic hyperventilation, bicarbonate and potassium levels may be decreased because of increased renal excretion (Pearson et al 1986). Finally, stress can produce a hyperadrenergic state that may trigger hyperventilation through beta-adrenergic stimulation (Magarian 1982).

Central and peripheral mechanisms have been postulated for production of neurologic symptoms during hyperventilation (Beumer and Bruyn 1993). Voluntary hyperventilation can reduce cerebral blood flow by 30% to 40% (Gotoh et al 1965; Jibiki et al 1992). 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 the elderly. A brainstem-mediated response to hypocarbia has been proposed (Patel and Maulsby 1987). The response may be due to metabolic rather than just hemodynamic factors (Kraaier et al 1992). **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 rate of fall of pCO₂ and the onset of dizziness and [paresthesias](#) suggests that symptoms may be due to hypophosphatemia ([Rafferty et al 1992](#)). Hypophosphatemia can result in symptoms such as tiredness, 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 Ca²⁺ may increase peripheral nerve axonal excitability, resulting in spontaneous bursting activity of cutaneous axons, perceived as paresthesias ([Macefield and Burke 1991](#)). [Lateralization](#) of symptoms might be explained by anatomic differences in the peripheral nerves and their nutrient vessels ([Galín et al 1977](#)).

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](#) ([O'Sullivan et al 1992](#)). Although anatomic differences in the cerebral vasculature might explain the unilateral paresthesias, normal magnetic resonance angiographic findings in 2 cases argue against this ([Evans 1995](#)). Additionally, there is a single report of asymmetrically decreased cerebral blood flow with decreased flow in the right parietal area with left-sided symptoms ([Evans 1995](#)).

It is not known why unilateral paresthesias occur more often on the left side of the face and body. One hypothesis is that psychosomatic symptoms are associated with right hemisphere psychic processes. During stress and emotional arousal, the right hemisphere is activated more than the left ([Tucker et al 1977](#)). Symptoms of conversion or hyperventilation are more likely to occur on the left side of the face and body ([Galín et al 1977](#); [O'Sullivan et al 1992](#)). However, this hypothesis does not explain the increased frequency of left-sided paresthesias in normal subjects who are asked to hyperventilate.

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Epidemiology

Hyperventilation syndrome occurs in about 6% to 11% of the general patient population ([Brashear 1983](#)). In a clinic that evaluated patients with [dizziness](#), hyperventilation syndrome accounted for 24% of the cases ([Drachman and Hart 1972](#)). Most studies have reported hyperventilation syndrome occurring 2 to 7 times more frequently in women than in men, with most patients ranging in age between 15 and 55 years ([Garssen and Rijken 1990](#)). One large study reported that patients with acute hyperventilation syndrome ranged in age from 5 to 85 years and was particularly prevalent in women in their late teens ([Hirokawa et al 1995](#)). The prevalence of chronic hyperventilation is highest in middle-aged women ([Hirokawa et al 1995](#)). In studies of patients with neurologic symptoms of hyperventilation syndrome, the percentage of females ranges from 50% ([Blau et al 1983](#)) to 67% ([Perkin and Joseph 1986](#); [Brodtkorb et al 1990](#); [O'Sullivan et al 1992](#)) to 87% ([Pincus 1978](#)).

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Prevention

For psychogenic cases of hyperventilation syndrome, avoidance of triggers is a preventative measure.

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Differential diagnosis

Hyperventilation syndrome has organic and physiological as well as emotional and habitual causes. Less than 5% of hyperventilation has a solely organic cause, 60% has a psychogenic (emotional and habitual) basis, and the remainder has varying combinations ([Brashear 1984](#)). The variety of organic disorders that can result in hyperventilation

include: (1) effects of salicylate, caffeine, [topiramate](#) ([Laskey et al 2000](#)), and other drugs; (2) cirrhosis and hepatic [coma](#); (3) acute pain such as that accompanying a myocardial infarction; (4) splenic flexure syndrome, cholecystitis, fever, and [sepsis](#); and (5) [dissecting aortic aneurysm](#), respiratory dyskinesia, pulmonary [embolism](#), pneumothorax, interstitial lung disease, asthma, and heat and altitude acclimatization ([Brashear 1983](#); [Block and Szidon 1994](#)).

Neurologic disorders that may cause hyperventilation include Rett syndrome, [Joubert syndrome](#), Reye syndrome, pyruvate dehydrogenase deficiency, biotin-dependent multiple carboxylase deficiency, [malignant hyperthermia](#), brainstem tumor, primary cerebral lymphoma, [encephalitis](#), brainstem strokes, [thalamic hemorrhage](#), syringobulbia, and neurogenic pulmonary edema due to intracranial hypertension ([Beumer and Bruyn 1993](#)). Severe hyperventilation can occur in the absence of psychiatric, respiratory, neurologic, or other organic abnormalities ([Bass and Gardner 1985](#)).

In patients diagnosed with hyperventilation syndrome by neurologists, the misdiagnoses of referring physicians have included [epilepsy](#), [migraine](#), [multiple sclerosis](#), [arteriovenous malformation](#), cerebrovascular disease, [vertebrobasilar insufficiency](#), [brachial neuritis](#), angina, malingering, vasovagal attacks, functional illness, [hypoglycemia](#), and cerebral tumor ([Blau et al 1983](#); [Perkin and Joseph 1986](#)). Hyperventilation might also contribute to some of the manifestations of migraine such as [syncope](#).

Cardiac abnormalities should certainly be considered in those patients with chest pain. The distinction between angina and hyperventilation syndrome at times is difficult because hyperventilation can produce electrocardiogram changes including T-wave inversions, systolic time-segment depression, and systolic time-segment elevation in patients without coronary artery disease ([Heckerling and Hanashiro 1985](#)). Some patients with angina may hyperventilate in response to their pain and anxiety. The symptoms of mitral valve prolapse and hyperventilation syndrome overlap. In some patients, symptoms may be due to hyperventilation ([Tavel 1990](#)).

The symptoms of panic attacks greatly overlap with hyperventilation syndrome, and the differential diagnosis is quite similar ([Tesar and Rosenbaum 1993](#); [Stahl and Soefje 1995](#)). The pathophysiology of panic attacks is controversial; hyperventilation syndrome has been suggested as a cause ([Ley 1985](#); [Nutt and Lawson 1992](#); [Folgering 1999](#)). Patients diagnosed with panic attacks that report brief episodic unilateral [paresthesias](#) or weakness may have the neurologic symptoms reproduced with the hyperventilation test ([Coyle and Serman 1986](#)).

Tonic spasms (paroxysmal [dystonia](#)) of multiple sclerosis can be somewhat similar to the muscle spasms, tetany, and paresthesias of hyperventilation syndrome. The episodes consist of brief, recurrent, often painful abnormal posturing of 1 or more extremities without alteration of consciousness, loss of sphincter control, or clonic movements. They last for 10 seconds to 3 minutes and recur as often as 30 times daily. Some patients may experience brief sensory disturbances in the involved extremity before or during the attack. Because the episodes can be the initial presentation of multiple sclerosis ([Heath and Nightingale 1982](#)) and can be triggered by hyperventilation ([Shibasaki and Kuroiwa 1974](#)), diagnostic confusion might result.

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Diagnostic workup

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 750 mL per minute may lead to overbreathing that is not easily detectable. Because the chronic disorder is intermittent, spot arterial [pCO₂](#) or end tidal volume [pCO₂](#) 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 1 or 2 symptoms but, on performing the hyperventilation provocation test, report other symptoms that appear during their typical episodes 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 3 minutes (Lum 1987). Based on a study of healthy subjects, a minimum duration of 3 minutes and end-tidal pCO₂ decreasing to at least 1.9 kPa or dropping well over 50% of baseline should elicit symptoms in most people (Hornsveld et al 1995). Dizziness, unsteadiness, and blurred vision commonly develop within 20 to 30 seconds, especially with the patient in the standing position; paresthesias start later (Lum 1987). Chest pain is reported by 50% of patients after 3 minutes of hyperventilation and by all by 20 minutes (Evans and Lum 1977). For clinical purposes, measurement of end tidal volume pCO₂ is not necessary. In addition, there is no clear correlation between paCO₂ and neurologic signs (Stoop et al 1986). The hyperventilation provocation test should not be performed in patients with ischemic heart disease, cerebrovascular disease, pulmonary insufficiency, hyperviscosity states, significant anemia, sickle cell disease, or uncontrolled hypertension (Brashear 1983).

For some patients with hyperventilation syndrome, symptoms cannot be reliably reproduced during the hyperventilation provocation test or even on consecutive tests (Hirokawa et al 1995). In some cases, the hyperventilation provocation test lacks test-retest reliability (Lindsay et al 1991). For others, antecedent anxiety and stress, not present during the test, may predispose to symptom formation, perhaps because of a hyperadrenergic state (Magarian 1982; Perkin and Joseph 1986). Different patterns of hyperventilation with different respiratory rates, tidal volumes, and durations may induce different symptoms (Grossman and De Swart 1984; Hornsveld et al 1995). 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 (Malmberg et al 2000).

A double-blind, placebo-controlled study found the hyperventilation provocation test to be invalid (Hornsveld et al 1996). Because hyperventilation seemed a negligible factor in the experience of spontaneous symptoms, Hornsveld and colleagues even recommended avoiding the term "hyperventilation syndrome." However, the study may be flawed because of the method of patient selection. Patients were referred because of a suspicion of hyperventilation syndrome and not based on reproduction of symptoms on a hyperventilation provocation test. Moreover, the presenting symptoms of subjects were not provided. Because the symptoms of hyperventilation syndrome can indeed be vague and nonspecific and because symptoms sometimes occur only with certain types of anxiety or stress, their conclusion may not apply to different population subsets (Naschitz et al 1996). The subjects' symptoms may have been due to chest wall pain or panic attacks.

Alternatively, the Nijmegen questionnaire (a list of 16 symptoms rated on a 5-point scale from never to very often) can be used to screen for hyperventilation syndrome. The efficacy of this questionnaire has been evaluated, revealing the sensitivity to be 91% and the specificity to be 95% (when using the clinical diagnosis based on the pattern of complaints as the gold standard) (van Dixhoorn and Duivenvoorden 1985). In a consecutive series of 100 patients in a neuro-otology practice, 23% of patients seen for vestibular assessment were diagnosed with hyperventilation syndrome; 74% of these would have potentially remained undetected had the Nijmegen questionnaire not been used (Humphriss et al 2004).

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 ([Gardner 2000](#)), is useful. In the individual case, if the hyperventilation provocation test fails to reproduce the symptoms but clinical suspicion persists, treatment such as breath holding, slow breathing, or breathing into a paper bag can certainly be suggested on a trial basis.

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Prognosis and complications

In a followup study of children and adolescents, 40% were still hyperventilating as adults and many suffered from chronic anxiety ([Herman et al 1981](#)). One half of patients with acute hyperventilation recover without treatment ([Hirokawa et al 1995](#)). In 10% of those with chronic hyperventilation, symptoms may persist for more than 3 years ([Hirokawa et al 1995](#)). With proper management, about 70% to 90% of adults become symptom-free ([Lum 1976](#); [Campernolle et al 1979](#)).

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Management

The various treatments for hyperventilation 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 ([Beumer and Bruyn 1993](#)). 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 8 sessions of breathing retraining ([Monday et al 1995](#)). A small pilot study found benefit from [acupuncture](#) ([Gibson et al 2007](#)). There is a lack of well-controlled treatment trials comparing these approaches ([Herxheimer 1991](#)).

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 the patient with written materials such as those used by Lance may be worthwhile ([Lance and Goadsby 2005](#)). If significant symptoms of stress, anxiety, or depression are present, use of appropriate medication and psychological or psychiatric referral may be helpful.

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Pregnancy

Although hyperventilation syndrome has often been seen during pregnancy, studies on the incidence are not available.

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Anesthesia

Not applicable.

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ICD codes

ICD-9:

Hyperventilation: 306.1

ICD-10:

Hyperventilation: R06.4

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Associated disorders

Acute hyperventilation

Anxiety

Chronic hyperventilation

Distal symmetrical [paresthesias](#)

Panic attacks

Raynaud phenomenon

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Related summaries

[Dizziness](#)

[Psychophysiological vertigo \(psychogenic vertigo\)](#)

[Syncope](#)

[Tension-type headache](#)

[Top ↑](#)

Differential diagnosis

[epilepsy](#)

[migraine](#)

[arteriovenous malformation](#)

[cerebrovascular disease](#)

[vertebrobasilar insufficiency](#)

[brachial neuritis](#)

[angina](#)

[malingering](#)

[vasovagal attacks](#)

[functional illness](#)

[hypoglycemia](#)

[cerebral tumor](#)

[cardiac abnormalities](#)

[mitral valve prolapse](#)

[panic attacks](#)

[multiple sclerosis](#)

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Demographics

For more specific demographic information, see the Epidemiology, Etiology, and Pathogenesis and pathophysiology sections of this clinical summary.

Age

[06-12 years](#)

[13-18 years](#)

[19-44 years](#)

[45-64 years](#)

[65+ years](#)

Population

None selectively affected.

Occupation

None selectively affected.

Sex

[female>male, >2:1](#)

[female>male, >1:1](#)

Family history

None

Heredity

None

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**References especially recommended by the author or editor for general reading.