**Background**

Hyperventilation syndrome (HVS) represents a relatively common ED presentation that is readily recognized by most clinicians. However, the underlying pathophysiology has not been clearly elucidated.

As classically defined, hyperventilation syndrome is a condition in which minute ventilation exceeds metabolic demands, resulting in hemodynamic and chemical changes that produce characteristic dysphoric symptoms. Inducing a drop in arterial pCO2 through voluntary hyperventilation reproduces these symptoms. Recently, however, this model has been challenged with the observation that many patients with hyperventilation syndrome do not manifest low arterial pCO2 levels during attacks. In some cases, patients with this syndrome have demonstrated altered respiratory physiology that is manifest as a slower return to baseline of the pCO2 after voluntary hyperventilation to a defined level of pCO2.

Current thinking suggests that the syndrome might better be termed*behavioral breathlessness* or *psychogenic dyspnea* with hyperventilation as a consequence rather than as a cause of the condition. It is also recognized that some patients may be physiologically at risk of developing psychogenic dyspnea.

Symptoms of hyperventilation syndrome and panic disorder overlap considerably, although the two conditions remain distinct. Approximately 50% of patients with panic disorder and 60% of patients with agoraphobia manifest hyperventilation as part of their symptomatology, whereas only 25% of patients with hyperventilation syndrome manifest [panic disorder](http://emedicine.medscape.com/article/287913-overview).

## Pathophysiology

Hyperventilation syndrome occurs in acute and chronic forms. Acute hyperventilation syndrome accounts for only 1% of cases but is more easily diagnosed. Chronic hyperventilation syndrome can present with a myriad of respiratory, cardiac, neurologic, or GI symptoms without any clinically apparent overbreathing by the patient. Hypocapnia can be maintained without any change in the absolute minute volume if the patient exhibits frequent sighs interspersed with normal respirations.

Because of the subtlety of hyperventilation, many patients with chronic hyperventilation syndrome are admitted and undergo extensive and expensive testing in an attempt to discover organic causes of their complaints.

The underlying mechanism by which some patients develop hyperventilation is unknown. One theory suggests that certain stressors provoke an exaggerated respiratory response. Several such stressors have been identified, including emotional distress, sodium lactate, caffeine, isoproterenol, cholecystokinin, and CO2. Predisposition to hyperventilation syndrome may also be rooted in childhood. Patients with hyperventilation syndrome were shown to have a higher percentage of overprotective parents when they were children. A sudden stressful situation later in life can then incite the first episode of hyperventilation syndrome.[1]

Infusion of lactate provokes symptoms of panic in 80% of patients with panic disorder but in only 10% of controls. Approximately one half of the lactate responders develop acute hyperventilation as part of the panic reaction. Lactate levels are higher and remain elevated longer in patients with panic disorder than in controls, suggesting that abnormal metabolism of lactate is involved in the pathogenesis, although the exact abnormality has not been characterized. Whether the same abnormality is operant in pure hyperventilation syndrome is unknown. In addition, elevated levels of carbon dioxide have been shown to induce panic symptoms in a majority of patients with panic disorder. Those patients who panicked with increased carbon dioxide had significantly greater baseline respiratory variability, which is also found in patients with hyperventilation syndrome, further suggesting a connection between the two.[2]

The explanation of hyperventilation syndrome lies partially in the mechanics of breathing. Normal tidal volumes range from 35-45% of vital capacity at rest. The elastic recoil of the chest wall resists hyperinflation of the lungs beyond that level, and inspiratory volumes beyond this level are perceived as effort or dyspnea. Patients with hyperventilation syndrome tend to breathe by using the upper thorax rather than the diaphragm, resulting in chronically overinflated lungs. When stress induces a need to take a deep breath, the deep breathing is perceived as dyspnea. The sensation of dyspnea creates anxiety, which encourages more deep breathing, and a vicious cycle is created.

Another common theory is that patients with panic disorder have a lower threshold for the fight or flight response. In patients who are susceptible, even minor stresses can trigger the syndrome, which then tends to manifest with primarily psychiatric complaints, such as fear of death, impending doom, or claustrophobia. In contrast, it is believed that patients with hyperventilation syndrome tend to focus on somatic complaints related to the physiologic changes produced by hyperventilation. The initiating stimulus and the abnormal stress response may be identical in each group but are expressed differently.

## Epidemiology

### Frequency

#### United States

As many as 10% of patients in a general internal medicine practice are reported to have hyperventilation syndrome as their primary diagnosis, although equivalent data are not available for ED presentations. It is thought that up to 6% of the general population exhibits aspects of hyperventilation syndrome.

### Mortality/Morbidity

Death attributable to the syndrome is extremely rare. A leftward shift in the HbO2 dissociation curve and vasospasm related to low pCO2 could cause myocardial ischemia in patients with coronary artery disease and hyperventilation syndrome.

Certain patients are disabled psychologically by their symptoms, and many patients carry false diagnoses. Patients with hyperventilation syndrome often undergo unnecessary testing and suffer from the complications of these interventions (eg, angiography, thrombolytics, nasal reconstruction).[3]Withholding such therapy may be difficult in a patient with crushing chest pain and dyspnea.

One study reported a series of 45 patients with chest pain who had normal coronary arteries on angiography. These patients ultimately were diagnosed as having hyperventilation syndrome. Over a 3.5-year average follow-up period, 67% of the patients had made subsequent ED visits for chest pain, and 40% of the patients had been readmitted to rule out myocardial infarction.

Clearly, hyperventilation syndrome not only produces severe and genuine discomfort for the patient it also accounts for considerable medical expense in excluding more serious pathology. The fact that patients with hyperventilation syndrome appear ill prompts further esoteric testing, which is inevitably nondiagnostic; the chronicity of the condition often prompts different physicians to repeat these unnecessary investigations.

### Sex

A female preponderance of hyperventilation syndrome exists; the female-to-male ratio may be as high as 7:1.

### Age

The peak age of incidence is from 15-55 years, but cases have been reported in all age groups except infancy.

## History

Patients with acute hyperventilation syndrome (HVS) may present with great agitation and anxiety.

Most commonly, the history is of sudden onset of dyspnea, chest pain, or neurologic symptoms (eg, dizziness, weakness, paresthesias, near syncope) following a stressful event.

Patients with chronic hyperventilation syndrome present with similar symptoms, including recurrent chest pain, dyspnea, and neurologic deficits, and usually have many similar presentations in the past.

### Acute hyperventilation

Patients often present dramatically with agitation, hyperpnea and tachypnea, chest pain, dyspnea, wheezing, dizziness, palpitations, tetanic cramps (eg, carpopedal spasm), paresthesias, generalized weakness, and [syncope](http://emedicine.medscape.com/article/811669-overview).

The patient often complains of a sense of suffocation. An emotionally stressful precipitating event often can be identified.

An emotionally stressful precipitating event can often be identified.

### Cardiac symptoms

The chest pain associated with hyperventilation syndrome usually has atypical features, but, on occasion, it may closely resemble typical angina. It tends to last hours rather than minutes, and is often relieved rather than provoked by exercise.

It is usually unrelieved by nitroglycerin.

The diagnosis of hyperventilation syndrome should be considered in young patients without cardiac risk factors who present with chest pain, particularly if associated with paresthesias and carpopedal spasm. However, this diagnosis should be reached cautiously, because many other potentially lethal conditions can cause young patients to present with chest pain (eg,[pulmonary embolism](http://emedicine.medscape.com/article/300901-overview%22%20%5Ct%20%22_self), [spontaneous pneumothorax](http://emedicine.medscape.com/article/424547-overview)).

ECG changes are common in patients with hyperventilation syndrome. Abnormalities may include prolonged QT interval, ST depression or elevation, and T-wave inversion.

In patients with subcritical coronary artery stenosis, the vasospasm induced by hypocarbia may be sufficient to provoke myocardial injury.

The incidence of hyperventilation syndrome is high among patients with mitral valve prolapse (MVP), and the chest pain associated with MVP may be due to hyperventilation.

Prinzmetal angina (ie, coronary angiospasm) is triggered by hyperventilation syndrome, but the chest pain associated with this syndrome normally would be expected to respond to nitrates or calcium channel blockers.

### Central nervous system symptoms

CNS symptoms occur because hypocapnia causes reduced cerebral blood flow (CBF). CBF decreases 2% for every mm Hg decrease in pCO2.

Symptoms of dizziness, weakness, confusion, and agitation are common.

Patients may report feelings of depersonalization and may experience visual hallucinations.

Syncope or seizure may be provoked by hyperventilation.[4]

Paresthesias occur more commonly in the upper extremity and are usually bilateral.

Perioral numbness is very common.

### GI symptoms

GI symptoms (eg, bloating, belching, flatus, epigastric pressure) may result from aerophagia.

### Metabolic changes

Acute metabolic changes result from intracellular shifts and increased protein binding of various electrolytes during respiratory alkalosis.

Acute secondary hypocalcemia can result in carpopedal spasm, muscle twitching, prolonged QT interval, and positive Chvostek and Trousseau signs.

Hypokalemia tends to be less pronounced than hypocalcemia but can produce generalized weakness.

Acute secondary hypophosphatemia is common and may contribute to paresthesias and generalized weakness.

### Chronic hyperventilation

The diagnosis of chronic hyperventilation syndrome is much more difficult than that of acute hyperventilation syndrome because hyperventilation is usually not clinically apparent.

Often, these patients have had extensive medical investigations and have been assigned several misleading diagnoses.

Two thirds of patients with chronic hyperventilation syndrome have a persistently slightly low pCO2 with compensatory renal excretion of HCO3, resulting in a near-normal pH level. These patients tend to have more prominent CNS symptoms than patients who maintain normal pCO2 during attacks. These patients usually present due to dyspnea and chest pain.

The respiratory alkalosis can be maintained with occasional deep sighing respirations, which are observed often in patients with chronic hyperventilation syndrome.

When faced with an additional stress that provokes hyperventilation, the physiologic acid-base reserve is less, and these patients become symptomatic more readily than patients without hyperventilation syndrome.

### Other

Dry mouth occurs with mouth breathing and anxiety.

Many of these patients suffer from obsessive-compulsive disorders, experience sexual and marital difficulties, and have poor adaptations to stress.

Patients with chronic hyperventilation syndrome may have symptoms that mimic virtually any serious organic disorder, but they usually have atypical features of these diseases.

## Physical

### Acute hyperventilation

Obvious tachypnea and hyperpnea are present.

Although chest wall tenderness is common in patients with hyperventilation syndrome, the finding is not helpful, because chest wall tenderness also is found in pneumonia, pneumothorax, pulmonary embolism, coronary artery syndromes, and a wide variety of other serious and benign thoraco-abdominal diseases.

Carpopedal spasm occurs when acute hypocarbia causes reduced ionized calcium and phosphate levels, resulting in involuntary contraction of the feet or (more commonly) the hands.

Chvostek or Trousseau signs may be positive because of [hypocalcemia](http://emedicine.medscape.com/article/767260-overview%22%20%5Ct%20%22_self).

Wheezing may be heard because of bronchospasm from hypocarbia.

Tremor, mydriasis, pallor, tachycardia, and other manifestations of anxiety can occur.

Evidence of depersonalization or hallucination may be noted.

### Chronic hyperventilation syndrome

Hyperventilation is usually not readily apparent.

Frequent sighing respirations, 2-3 per minute and frequent yawning are noted.

Chest wall tenderness, numbness, and tingling may be present.

Characteristically, patients have multiple complaints without much supporting physical evidence of disease.

## Causes

The cause of hyperventilation syndrome is unknown, but some persons who are affected appear to have an abnormal respiratory response to stress, sodium, lactate, and other chemical and emotional triggers, thereby resulting in excess minute ventilation and hypocarbia. In most patients, the mechanics of breathing are disordered in a characteristic way. When stressed, these patients rely on thoracic breathing rather than diaphragmatic breathing, resulting in a hyperexpanded chest and high residual lung volume. Because of the high residual volume, they are then unable to take a normal tidal volume with the next breath and consequently experience dyspnea. Proprioceptors in the lung and chest wall signal the brain with a "suffocation alarm" that triggers release of excitatory neurotransmitters that are responsible for many of the symptoms such as palpitations, tremor, anxiety, and diaphoresis.

The incidence of hyperventilation syndrome in first-degree relatives is higher than in the general population, but no clear genetic factors have been identified.

**Differentials**

* Acute Respiratory Distress Syndrome
* [Asthma](http://emedicine.medscape.com/article/296301-overview)
* [Atrial Fibrillation](http://emedicine.medscape.com/article/151066-overview)
* [Atrial Flutter](http://emedicine.medscape.com/article/757549-overview)
* [Cardiomyopathy, Dilated](http://emedicine.medscape.com/article/348284-overview)
* [Cardiomyopathy, Restrictive](http://emedicine.medscape.com/article/348745-overview)
* [Chronic Obstructive Pulmonary Disease and Emphysema](http://emedicine.medscape.com/article/807143-overview)
* [Costochondritis](http://emedicine.medscape.com/article/212029-overview)
* [Diabetic Ketoacidosis](http://emedicine.medscape.com/article/118361-overview)
* [Hyperventilation Syndrome](http://emedicine.medscape.com/article/807277-overview)
* [Metabolic Acidosis](http://emedicine.medscape.com/article/768268-overview)
* [Methemoglobinemia](http://emedicine.medscape.com/article/815613-overview)
* [Myocardial Infarction](http://emedicine.medscape.com/article/155919-overview)
* [Nasopharyngeal Stenosis](http://emedicine.medscape.com/article/861554-overview)
* [Panic Disorders](http://emedicine.medscape.com/article/287913-overview)
* [Pleural Effusion](http://emedicine.medscape.com/article/807375-overview)
* [Pneumonia, Bacterial](http://emedicine.medscape.com/article/300157-overview)
* [Pneumothorax, Iatrogenic, Spontaneous and Pneumomediastinum](http://emedicine.medscape.com/article/424547-overview)
* [Pneumothorax, Tension and Traumatic](http://emedicine.medscape.com/article/424547-overview)
* [Pulmonary Embolism](http://emedicine.medscape.com/article/300901-overview)
* [Respiratory Distress Syndrome, Adult](http://emedicine.medscape.com/article/165139-overview)
* [Smoke Inhalation](http://emedicine.medscape.com/article/771194-overview)
* [Toxicity, Carbon Monoxide](http://emedicine.medscape.com/article/819987-overview)
* [Toxicity, Carbon Monoxide](http://emedicine.medscape.com/article/1009092-overview)
* [Venous Air Embolism](http://emedicine.medscape.com/article/761367-overview)
* [Withdrawal Syndromes](http://emedicine.medscape.com/article/819502-overview)

## Laboratory Studies

Upon a first attack of acute hyperventilation syndrome, the diagnosis depends on recognizing the typical constellation of signs and symptoms and ruling out the serious etiologies that can cause the presenting symptoms.

Acute coronary syndrome and pulmonary embolism are the two most common serious entities that may present in a similar way to hyperventilation syndrome. Usually, clinical assessment is sufficient to rule these out. Depending on that assessment, more specific testing is sometimes warranted.

A standard workup for atypical chest pain, including pulse oximetry, chest radiography, and ECG, may still be warranted depending on the clinical picture.

Patients with a history of hyperventilation syndrome who have undergone an appropriate workup at some earlier time may not need any further laboratory evaluation in the setting of a recurrence. Recognition of the typical constellation of dyspnea, agitation, dizziness, atypical chest pain, tachypnea and hyperpnea, paresthesias, and carpopedal spasm in a young, otherwise healthy patient with an adequate prior evaluation is sufficient to make the diagnosis.

A low pulse oximetry reading in a patient who is hyperventilating should never be attributed to hyperventilation syndrome. The clinician should evaluate the patient for other causes of hyperventilation.

A normal pulse oximetry reading is not helpful because a severe defect in gas exchange can easily be masked by hyperventilation. A fraction of patients with chronic pulmonary embolism will have compensated chronic hyperventilation that may mimic primary chronic hyperventilation.

### Arterial blood gas measurement

An [arterial blood gas (ABG) measurement](http://emedicine.medscape.com/article/1982163-overview) is indicated if any doubt exists as to the patient's underlying respiratory status; it may be helpful when HVS-induced acidosis is suspected, or when shunting or impaired pulmonary gas exchange is considered.

ABG sampling confirms a compensated respiratory alkalosis in a majority of cases. The pH is typically near normal, with a low pCO2 and low HCO3.

ABG is also useful in ruling out [toxicity from carbon monoxide poisoning](http://emedicine.medscape.com/article/819987-overview), which may present in a similar fashion to HSV.[5]

### Other tests

Toxicology screen is indicated.

If acute pulmonary embolism is being considered, a quantitative enzyme-linked immunosorbent assay (ELISA) D-dimer assay may be helpful.

## Imaging Studies

Imaging studies are not indicated when the diagnosis of hyperventilation syndrome is clear.

In less obvious cases of hyperventilation syndrome, imaging studies are typically normal.

Because pulmonary embolism can present with findings identical to those of hyperventilation syndrome, a first-ever episode of acute HVS may warrant a V/Q scan or computed tomography pulmonary angiogram to rule out perfusion defects.

Chest radiography is indicated for patients at high risk of cardiac or pulmonary pathology. Chest radiography is also indicated when the diagnosis is not clear.

## Other Tests

### ECG

Changes are common and may include the following:

* ST depression or elevation
* Prolonged QT interval
* T-wave inversion
* Sinus tachycardia

### Orthostatic respiratory rate changes

Respiratory rate typically increases in the normal individual when going from supine to standing.

Patients with HVS have an accentuated increase in minute ventilation.

End tidal CO2 was found to be significantly lower in patients with HVS.

Ventilatory equivalents for O2 and CO2 were significantly higher in patients with HVS.

Noninvasive measurements of gas exchange during orthostatic testing are therefore useful in the diagnosis of patients with HVS.

## Prehospital Care

Because respiratory distress or chest pain has many potentially serious causes, this diagnosis should never be made in the field. Even when a patient carries a prior diagnosis of hyperventilation syndrome (HVS), it is still necessary to transport patients with these complaints to a hospital for a more complete evaluation.

Rebreathing into a paper bag is not recommended in the field.

Deaths have occurred in patients with acute myocardial infarction (MI), pneumothorax, and pulmonary embolism who were initially misdiagnosed with HVS and treated with paper bag rebreathing.

## Emergency Department Care

ED treatment of hyperventilation syndrome is often ineffective. Techniques of rebreathing into a paper bag are no longer recommended because significant hypoxia and death have been reported.

In patients who are hyperventilating for organic reasons (eg, pulmonary edema, [metabolic acidosis](http://emedicine.medscape.com/article/768268-overview)), increasing pCO2 and decreasing O2 may be disastrous.

In addition, paper bag rebreathing is often unsuccessful in reversing the symptoms of HVS because patients have difficulty complying with the technique. Moreover, CO2 itself may be a chemical trigger for anxiety in these patients.

Once life-threatening conditions are eliminated, simple reassurance and an explanation of how hyperventilation produces the patient's symptoms is usually sufficient to terminate the episode.

Provoking the symptoms by having the patient voluntarily hyperventilate for 3-4 minutes often convinces the patient of the diagnosis but is time-consuming and may be ineffective.

Most patients with hyperventilation syndrome tend to breathe using the upper thorax and have hyperinflated lungs throughout the respiratory cycle. Because the residual lung volume is high, the patient is unable to take a full tidal volume and experiences dyspnea. Physically compressing the upper thorax and having the patient exhale maximally decreases hyperinflation of the lungs. Instructing the patient to breathe abdominally, using the diaphragm more than the chest wall, often leads to improvement in subjective dyspnea and eventually corrects many of the associated symptoms.

Diaphragmatic breathing slows the respiratory rate, gives the patient a distracting maneuver to perform when attacks occur, and gives the patient a sense of self-control during the episode. This technique has been shown to be very effective in a high proportion of patients with hyperventilation syndrome.

Patients should be referred to a specialist (eg, physiotherapist, psychologist, psychiatrist, family physician, internist, respiratory therapist) who can reinforce this approach.

Use of benzodiazepines for stress relief and for resetting the trigger for hyperventilation is effective, but patients may require prolonged treatment.

Although acute chemical sedation may be effective and humane in selected severe cases, prolonged use of these medications should not be initiated in the ED.

Stress reduction therapy, beta-blockers, and breathing retraining all have proven effective in reducing the intensity and the frequency of episodes of hyperventilation. If the diagnosis of hyperventilation syndrome has been established, the patient should be referred to an appropriate therapist to implement these techniques over the long term.

## consultations

Acute consultation usually is not required. The patient can be referred to the primary physician or to a therapist to help control this disease.

## Medication Summary

Benzodiazepines are effective in reducing stress that may provoke hyperventilation syndrome (HVS) and are thought to reset the CNS response to a variety of "panicogens."

Selective serotonin reuptake inhibitors have been reported to reduce the frequency and the severity of episodes of hyperventilation.

## Benzodiazepines

### Class Summary

These agents are useful in the treatment of hyperventilation resulting from anxiety and panic attacks. By binding to specific receptor sites, these agents appear to potentiate the effects of gamma-aminobutyrate (GABA) and to facilitate inhibitory GABA neurotransmission and other inhibitory transmitters.

### [Alprazolam (Xanax)](http://reference.medscape.com/drug/xanax-niravam-alprazolam-342896)

Indicated for treatment of anxiety and management of panic attacks.

### [Lorazepam (Ativan)](http://reference.medscape.com/drug/ativan-loraz-lorazepam-342906)

Sedative hypnotic in benzodiazepine class that has short onset of effect and relatively long half-life. By increasing action of GABA, a major inhibitory neurotransmitter, may depress all levels of CNS, including limbic and reticular formation.

## Selective serotonin reuptake inhibitors

### Class Summary

These agents are useful in treating hyperventilation associated with anxiety.

### [Paroxetine (Paxil)](http://reference.medscape.com/drug/paxil-paxil-cr-paroxetine-342959)

Alternate DOC; potent selective inhibitor of neuronal serotonin reuptake. Has weak effect on norepinephrine and dopamine neuronal reuptake.

## Further Inpatient Care

Inpatient care is not indicated, but many patients with chronic hyperventilation syndrome (HVS) are admitted because their symptomatology resembles many serious organic problems and because no simple way to confirm the diagnosis in the ED is available.

## Further Outpatient Care

Patients should be referred to a consultant psychiatrist, psychologist, or family physician with expertise and interest in managing HVS. Some physiotherapists and respiratory therapists have extensive experience in retraining patients in proper breathing techniques and should be consulted.

Patients may also be referred for treatment with acupuncture. This modality is useful in reducing anxiety levels, thereby reducing the severity of symptoms associated with HVS. By reducing anxiety, the frequency of symptomatic periods may also be reduced.[7]

**Inpatient & Outpatient Medications**

Several medications, including benzodiazepines and SSRIs, are effective in reducing the frequency and the severity of hyperventilation. These agents require prolonged use and are best managed by a consultant on an ongoing outpatient basis rather than through sporadic prescriptions following an ED visit.

## Complications

Complications are related mainly to invasive procedures and investigations (eg, angiography) that are used in the workup of hyperventilation syndrome. Complications are also a result of symptoms produced indirectly by hyperventilation (eg, injuries sustained in a fall during a syncopal episode due to hyperventilation).

## Prognosis

Patients with chronic HVS experience multiple exacerbations throughout their lives.

Children who experience acute hyperventilation often continue this pattern into adulthood.

Many patients have associated disorders (eg, agoraphobia) that may dominate the clinical picture.

Management of these underlying disorders affects the course of hyperventilation.

Patients who are treated with breathing retraining, stress reduction therapy, and various medications (eg, benzodiazepines, SSRIs) experience significant reductions in the frequency and the severity of exacerbations.

## Patient Education

Patients should have the underlying pathophysiology explained and should be instructed in the technique of deflating the upper chest followed by controlled diaphragmatic breathing.

For excellent patient education resources, visit eMedicine's [Anxiety Center](http://www.emedicinehealth.com/collections/CO1587.asp). Also, see eMedicine's patient education articles, [Anxiety](http://www.emedicinehealth.com/articles/18885-1.asp), [Panic Attacks](http://www.emedicinehealth.com/articles/18973-1.asp), and[Hyperventilation](http://www.emedicinehealth.com/articles/18951-1.asp).