The hyperventilation syndrome is usually easily recognized when it follows an acute and typical form. This diagnosis is often missed, however, when it is overshadowed by secondary physical sensations, or follows a chronic and insidious course [1,2]. The major clinical manifestations of hyperventilation syndrome [3] generally include one or more of the symptoms of breathlessness out of proportion to physical effort, chest pain usually not typical of angina pectoris, dizziness, paresthesias, weakness, fatigue, and palpitations. Anxiety initiates the excessive breathing, which then results in hypocapnia, respiratory alkalosis and a complex sequence of physiologic changes [4], responsible for most of the signs and symptoms; these changes may even produce broncho constriction that may actually result in audible wheezing, augmenting the sensation of dyspnea as well as simulating or intensifying preexisting asthma [5].

For most people, hyperventilation is rare and only occurs as an occasional response to fear or stress. For others, this condition occurs regularly as a typical response to emotional excesses such as depression, anxiety, or anger. When hyperventilation is a frequent occurrence, it is known as hyperventilation syndrome.

How emotional stress induces such a respiratory response is unclear, but it is likely rooted in the evolutionary “flight or fight” reaction, wherein, in anticipation of imminent increased exertion combined with increased adrenergic drive, rapid respiration results. If such exertion is not required, however, this response becomes disproportionally great, setting in motion the undesirable chain of events noted in this report.

Because of rapid mouth breathing, the sensation of dryness of the mouth is a regular feature. The chest pain is often variable in nature, lasting from minutes to hours, often sharp and migratory; but it may occasionally resemble a cardiac origin. The sensation of dizziness, or giddiness, sometimes resembles true vertigo, and may culminate in unconsciousness and resemble seizures, suggesting diseases that cause syncope or vestibular dysfunction. Symptoms may also be aggravated by upright posture, suggesting orthostatic hypotension. Although the somatic sensations of numbness and tingling (paresthesias) are typically perioral in location, more often they affect the arms, hands, legs, and feet, occasionally dominant or exclusively localized to one side of the body usually the left [6], simulating a neurologic disorder. Additional symptoms include hot sensations, sometimes with diaphoresis, and feelings of chilliness. These sensations likely result from adrenergic stimulation combined with peripheral vasomotor changes. Musculoskeletal pains and spasms, similar to those noted in the chest, may also occur in a variety of locations, such as the head and back. Nausea and symptoms consistent with aerophagia and globus hystericus are also commonly associated with the anxiety and rapid breathing. Hyperventilation produces sinus tachycardia and other electrocardiographic changes [7-9], most commonly downward shifts of ST segments with flattening of the T waves in the left precordial leads together with an apparent prolongation of the QT interval, changes resembling those of hypokalemia. Isolated T wave inversions and marked ST depressions are less common. The ST shifts can closely simulate cardiac ischemic changes, but they are usually not induced or are even lessened by exercise.

The patient him/herself may overlook the original over breathing, having become preoccupied with the associated somatic symptoms, and frequently complain that they often
cannot get a "deep enough breath," and they may sigh repeatedly while being interviewed, with predominately thoracic rather than abdominal respiration, often describing themselves as being anxious and depressed [10].

In many other instances of hyperventilation, bizarre unexplained somatic symptoms in virtually any area may dominate the picture and appear more severe than any demonstrable organic disease. Under these circumstances, the clinician must carefully seek associated signs that can allow for suspicion of the underlying hyperventilation [11].

Previous studies indicate that hyperventilation syndrome is quite common [1]; it has been observed in 5 to 10 percent of patients presenting to family practitioners and general internists, with significant numbers seen by consulting cardiologists and gastroenterologists. In my personal experience in evaluating applicants for permanent disability status, I estimated a frequency of approximately 15%. Despite such a high prevalence, this syndrome is regularly overlooked by all physicians, possibly attributable to an inordinate preoccupation with associated apparently physical symptoms. Such apparent bodily discomforts often prompt a referral to various subspecialists, who dismiss these patients as having no conditions falling within their special interest. This common sequence accords well with the author's experience in a practice involved primarily in internal medicine and cardiology.

Panic attacks (panic disorder)

It was not until 1980 that the specific concept of the panic disorder was designated as a psychological diagnosis [12]. According to the latest psychiatric handbook, DSM-5 [13], diagnostic criteria for a panic attack include a discrete period of intense fear or discomfort, in which four (or more) of the following symptoms develop abruptly and reach a peak within minutes:

- Palpitations, and/or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensations of shortness of breath or being smothered
- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded, or faint
- De-realization (feelings of unreality) or depersonalization (being detached from oneself)
- Fear of losing control or going insane
- Sense of impending death
- Paresthesia (numbness or tingling sensations)
- Chills or hot flashes

Obviously, this list bears a striking resemblance to those symptoms already noted with the hyperventilation syndrome. But now most of them are being attributed to the panic disorder. In recent years, few authors have considered the possibility that hyperventilation could have caused many if not all of the multiple somatic symptoms. On the other hand, some [14], have recognized that panic attacks are inextricably associated with hyperventilation, in which the excessive breathing per se induces disagreeable somatic symptoms that cause further anxiety, resulting in a vicious cycle of more frequent and severe attacks. I believe this latter likelihood creates the urgent need for every clinician to consider hyperventilation in all cases labeled as having panic disorder as well as other conditions that present with any of these listed manifestations for which physical maladies are found wanting.

Although the hyperventilation per se can account for most if not all of these symptoms, some have stated that the reverse is true, i.e., the anxiety and panic create the various bodily sensations and thus the rapid breathing is merely a secondary phenomenon [15,16]. Information presented in this review, however, strongly militates against this premise.

The Relationship between Hyperventilation and Panic Syndrome to Non Cardiac Chest Pain

In as much as the hyperventilation syndrome is but one of many causes of chest pain, its importance as a causative factor in populations without cardiac disease is of special interest. For example, Beitman et al. [17], in a study of non-anginal chest pain, provided a typical description of coexisting hyperventilation/panic disorder without considering the possibility that hyperventilation could have been an underlying contributor, an association that had been commonly noted previously [18,19].

A number of researchers have also examined functional disability and persistence of symptoms in patients with chest pain and normal coronary arteries, and they have discovered that approximately 40% have panic disorder [20]. In following such patients for up to six years or more, at least 70% continue to have chest pain, which is often debilitating. Approximately half reported being unable to work due to their symptoms and their usual daily activities were limited by chest pain despite the supposedly reassuring finding of normal coronary angiograms. They usually continued to consult repeatedly with their physicians for the same complaints, frustrated that nobody seemed to understand the source of their plight. This is understandable; for in none of these instances was the possibility of hyperventilation sought to explain the mechanism of the chest pain, without which efforts to control this disorder would have been futile.

OTHER APPARENT CONDITIONS IN WHICH HYPERVENTILATION PLAYS A PROMINENT ROLE

Asthma

As noted above, hyperventilation may simulate or intensify asthma. Of importance, asthmatic attacks bear a disproportionally high relationship with both panic attacks and hyperventilation [14].

Neurologic disorders simulated by hyperventilation

The frequent occurrence of light-headed sensations, sometimes followed by syncope, often combined with paresthesias that can
be dominant on one side of the body, suggest the possibility of a neurologic disorder such as cerebral vascular thrombosis or transient ischemic attacks. Cardiac dysrhythmia as also may be suspected as an explanation for syncopal episodes. These latter symptoms, encountered by physicians such as neurologists and cardiologists, prompt the need careful assessment for associated clues for hyperventilation.

**Other apparent “physical” syndromes**

Several studies [21] have suggested that mitral valve prolapse, a common congenital disorder, might be associated with and possibly be the cause of a variety of symptoms, including atypical chest pain, palpitations, dyspnea, anxiety and panic attacks, and electrocardiographic repolarization changes. Autonomic dysfunction, characterized by a hyperadrenergic state, has even been thought to occur in a high percentage of those studied, further supporting the contention that mitral prolapse is part of an underlying multisystem organic disorder or “syndrome.” Wooley [22] has even suggested that mitral prolapse accounts for all the manifestations previously attributed to neurocirculatory asthenia, panic disorder, and autonomic dysfunction states, advancing the hypothesis that the mitral prolapse syndrome had superseded all these other diagnostic categories. Controlled studies, however, have not supported a relationship between mitral prolapse and most of these “associated” signs and symptoms [23]. Since hyperventilation is such a common disorder, one would anticipate its frequent and fortuitous coincidence with the mitral defect. The frequent concurrence of this combination would tend to support any preconceived misappraisision by a clinician who believes that mitral prolapse accounts for the variety of the typical findings associated with hyperventilation especially anxiety and chest pain.

**DIAGNOSIS AND TREATMENT**

First, given any of the manifold symptoms and signs noted above, it is incumbent on the clinician to suspect that the problem may be caused by hyperventilation, even if the breathing disorder is denied by the patient. Suspicion is especially important when the diagnosis of panic attacks is considered.

Given a high index of suspicion, the presence of underlying hyperventilation is usually easily confirmed. This is accomplished by reproducing many or all the symptoms after the patient is instructed to breathe rapidly and deeply for at least two or three minutes, or at least until some discomfort such as paresthesias or dizziness is experienced, which can be identified by the patient as being identical to some or all of those experienced during an actual episode. Once recognized, prevention and control of at least this part of the disorder are usually successful through explanation of symptom causation, combined, if necessary, with either breath holding or rebreathing into a paper bag. By allowing patients to understand the mechanism of production, these maneuvers not only relieve the symptoms but help to allay the underlying anxiety that initially triggered the attack. This can be reinforced even further by instructing them to try purposely hyperventilating at home, bringing on the typical symptoms, and then realizing how quickly they can be reversed by breath holding.

Curiously, the associated chest pains may not be reproduced in such a short time frame, requiring a lengthy period of over breathing to develop [24]. Alternatively, the chest pains may originate independently in the musculoskeletal system but intensified during an actual episode.

Although laboratory confirmation of this disorder with the use of respiratory testing for reduced blood and alveolar levels of CO₂ has been advocated [14], I consider this unduly complex and expensive, but such testing could be reserved for difficult cases. Similarly, treatment aimed at training of proper breathing techniques rather than this simple explanatory approach detailed above, could be reserved as a secondary measure.

Few systematic studies have sought to demonstrate a causative role for hyperventilation in producing and sustaining the panic attacks. One study, however [25], did demonstrate such a close relationship, providing a basis for treatment of both the breathing disorder and the panic state. In this instance, patients were provided a CO₂ sensor and an audio playback device. The patients were directed to perform repeated breathing sessions per day for 28 days in their own homes. This treatment enabled patients to normalize their breathing patterns by controlling their respiratory rate and exhaled CO₂ as measured by the sensor. The results were striking, for after 12 months, 68% of patients were panic-attack free, 96% of patients had reported a significant reduction in their panic symptoms, and all patients experienced long-lasting reductions in panic attack frequency and severity, anxiety symptoms, and avoidance behaviors, all of which were coupled with improvements in mood and quality of life. If confirmed by similar studies, this could provide a major step toward diagnosis and management of most if not all panic syndromes. This observation accords well with the likelihood that the panic and hyperventilation are inextricably associated, providing a vicious cycle between the two, i.e., panic initiates hyperventilation, and symptoms from the latter then trigger more panic. As a practical matter, simple measures, as described above, will likely suffice to prevent and control the entire sequence of symptoms associated with panic in the vast majority of afflicted patients.

Treatment of the underlying anxiety can benefit this disorder through a pharmacologic approach with benzodiazepines, antidepressants, and cognitive behavioral therapy. Interestingly, however, those recommending such treatments [26] generally ignore the presence and potential benefit of the simplified breathing measures already presented.

**CONCLUSION**

Hyperventilation is one of the most commonly overlooked diagnoses in all of clinical medicine, baffling family practitioners, internists, and also several specialty groups as well, notably neurologists, cardiologists and psychiatrists. Although associated panic with extreme anxiety is usually obvious during the episodes, apparent somatic manifestations such as dizziness, weakness, chest pain, dry mouth, numbness and tingling often divert attention from the underlying breathing disorder. Patients often describe a feeling of shortness of breath, but may be totally unaware of such rapid respiration. Once suspected, simple measures of diagnosis and treatment usually suffice to prevent...
and control all the disagreeable bodily sensations as well as the underlying anxiety itself.

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