IM INTERNAL MEDICINE FOR THE SPECIALIST

Pulmonary Medicine

Hyperventilation and Cardiac Symptoms

By P. G. F. NIXON, F.R.C.P.

IN BRIEF

Hyperventilation that has an important role in cardiovascular symptoms is usually unobtrusive; it opposes order and control of autonomic stability and cardiovascular regulation. In generating respiratory alkalosis, hyperventilation promotes intracellular calcium ionization and, consequently, cardiac arrhythmia and coronary vasoconstriction or spasm. Thrombosis is encouraged. The outcome depends on the position of the patient on a performance-arousal curve, the chronicity of the overbreathing and its effect on the body's alkali-reserve systems, and the extent of the atherosclerotic handicap that may be present.

Health and survival depend on our ability to maintain a stable and orderly internal milieu in the face of an uncertain or changing external environment (1). By undermining cardiovascular stability and circulatory homeostasis at critical periods of strain, hyperventilation can reduce the capacity for making effort and cause cardiac arrhythmia, sudden death, coronary arterial spasm and constriction, myocardial infarction, and various neuroendocrine changes that militate against survival (2-4).

THE AROUSAL FACTOR

The simplest way for physicians to view hyperventilation is to imagine that the breathing controls have been uncoupled from the body's physical needs and attached to the mind's arousal system.

Figure 1 is an illustration of a performance-arousal curve (5). The upslope represents healthy function, in which the individual's performance can rise to meet the sum of demands imposed by the external environment and the intrinsic needs and intentions. The metabolic functions can be regarded as anabolic because the restoration of wear-and-tear processes and the maintenance of immune function are optimal. Some people have low curves, and the usual causes of this handicap are growing up in poverty (6), being overworked, and suffering the social disadvantages that militate against success in life and longevity (7-9).

Others are subjected to levels of arousal so high as to carry them beyond the limits of physiological tolerance. High levels of workload with insufficient control and lack of social support are commonly encountered in cardiovascular practice (10,11).

The peak of the performance-arousal curve represents the event or time that pushed the victim "over the top" and is followed by a downhill course (5), which usually lasts a year or two. There is an ever-increasing struggle to close the gap between the level of activity the individual can sustain and the higher level being sought. Healthy activity is replaced by feverish overwork accompanied by cycles of anger, frustration, and defeat. Catabolic disorders increase (Table I).

The physiological degradation (12) includes loss of effectiveness in performance,

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Hyperventilation

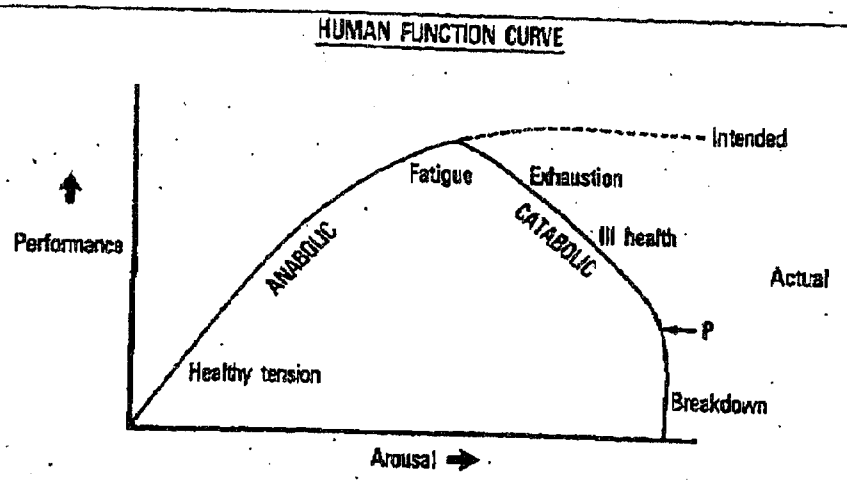

Figure 1. *A performance-arousal curve employed as a model in cardiac rehabilitation. Performance relates to coping ability and efficiency. Arousal relates to effort and, at the higher levels, to struggle. P represents the "catastrophic cliff edge" of instability where little further arousal is needed to precipitate a breakdown such as myocardial infarction or sudden death. Beyond the peak of physiological tolerance the metabolism changes from anabolic to catabolic and the individual deteriorates under the self-defeating struggle to close the gap between actual performance and the level he or she believes to be intended of him or her.* (Reproduced, with permission, from Nixon PGF *Practitioner 217:* 765-769, 935-944, 1976)

high emotionalism, difficulties of adaptation and habituation, maladaptive behavior and disturbance of social support systems, and catabolic distortion of the internal milieu. A hostile form of behavior caused by this distortion, colloquially termed *left hemispheric* (13), is thought to be associated with abnormal activation of the left sympathetic chain and, therefore, coronary vasoconstriction and malignant arrhythmia (14).

The role of hyperventilation in this scheme varies according to the performance-arousal curve. In healthy function, it serves to heighten arousal and is a transitory matter, capable of causing the chest to heave. During sexual arousal, hyperventilation can trigger the orgasm in a woman or cause premature ejaculation in a man. In those whose hyperventilation response is easily stimulated, the heart rate and blood-pressure responses to physical activity are increased and the neurohumoral consequences of anxiety are amplified. Hyperventilation has a strong adrenergic effect; this generates feelings of anxiety, which, in turn, stimulate breathing and initiate a vicious circle of increasing arousal that can cause such disorders as cardiac "neurosis" and mitral prolapse, phobic illness, and panic attacks. The role of hyperventilation and arousal in producing these disabilities has been identified by Soley and Shock (15): "the symptomatology and the biochemical and physiological changes which occur during hyperventilation have been reported adequately. It has been shown that the shift in the acid-base balance towards the alkaline side : . . is responsible for the symptoms. While hyperventilation might be caused by anoxaemia, organic nervous diseases, hot baths and hyperthermia, and anxiety and effort, we are most interested in the two causes last mentioned, since it has been recognized that the combination of anxiety and effort produces the symptoms listed variously under the diagnoses of 'soldier's heart,' 'disordered action of the heart,' 'neurocirculatory asthenia' and 'effort syndrome.'"

Thus, in tense situations, the hyperventilator goes over the top of the performance-arousal curve at lower levels of stimulation than does a nonhyperventilator.

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With time, the curve becomes ever lower. Spontaneous recovery is thought to take place in about 15 percent of cases.

THE CHRONICITY FACTOR

Chronicity alters the clinical presentation of hyperventilation. For reasons described below, muscular aches and pains and influenza-like symptoms tend to become more prominent than the cardiovascular symptoms, possibly because adrenal cortical activity waxes while adrenal medullary influence wanes. Misdiagnoses (e.g., Epstein-Barr virus, post-viral fatigue syndrome, or myalgic encephalomyelitis) are often made by physicians who are unfamiliar with the chemical and metabolic changes of chronic hyperventilation. Excellent reviews have been provided by Lum (16) and Magarian (17). These researchers describe the symptoms and disorders in every bodily system, and the emotional and cognitive abnormalities that result from chronic hyperventilation.

Transient hyperventilation causes hypocapnia and respiratory alkalosis, but chronic hyperventilation causes a great loss of carbon dioxide; the body would suffer metabolic alkalosis from loss of carbonic acid if it were not for the kidney's ability to excrete buffer-base reserves in order to maintain a normal pH. Unfortunately, this chronic loss of buffer-base reserves can produce a state in which the patient must hyperventilate in order to maintain pH normality and avoid acidosis (18). If this individual reduces breathing, he or she can become acidotic, which causes feelings of illness and restlessness and a compelling need to overbreathe again. This patient may be suffering from coronary insufficiency and cardiac arrhythmia due to hypocapnia but is not in a position to control the breathing disorder.

The quickest treatment is to reduce arousal with generous doses of sedation because arousal reduction greatly diminishes the impact of hyperventilation on the cardiovascular system. On the other hand, falling into deep sleep can depress the breathing and provoke acidosis, commonly at 3 or 4 A.M. (18). This acidosis stimulates overbrea-

FROM VICTORIA K

HYPERVENTILATION →	Hypocapnia →
Extracellular alkalosis	↑ Catecholamine release ↑ Sympathetic activity ↓ Vagal activity ↓ Oxygen uptake (Bohr) ↓ Potassium
Intracellular alkalosis →	Increased Ca^{++} →
Myocardium	↑ Systolic contraction ↓ Diastolic relaxation ↓ Compliance
Coronary vessels	Constriction and spasm
Electrocardiogram	Arrhythmia ST = segment and T-wave abnormalities
Thromboxane A_2	Vasoconstriction and thrombosis

Figure 2. *Some effects of hyperventilation-induced respiratory alkalosis on the cardiovascular system.*

thing to a degree that overshoots the target of pH regulation, induces hypocapnia, and can thereby cause the patient to waken with anxiety or panic, tachycardia and arrhythmia, nocturnal ischemia of the myocardium, or muscular stiffness and aching.

The chronic hyperventilator is entitled to weakness, stiffness, pain, or cramps of the skeletal muscles because the loss of buffer-base reserves renders them more acidic on effort; the loss of potassium and magnesium causes weakness, salt and water retention causes edema, and increasing calcium ionization promotes cramps. Another hallmark of chronic hyperventilation is restlessness. Standing still causes hypocapnia and stimulates the sympathoadrenal system. The result might be anxiety and panic or even tachycardia and coronary insufficiency.

The individual on the downslope of the performance-arousal curve is exposed to greater danger as he journeys down towards P, the trigger point for a cardiovascular catastrophe, because the power of hyperventilation to trigger a catastrophe increases as the body's homeostatic defenses decrease.

SHIFTS OF CARDIOVASCULAR EQUILIBRIA: ISCHEMIA AND ARRHYTHMIA

Figure 2 summarizes the more important cardiovascular changes induced by hyperventilation. Their influence is to shift vital equilibria in the direction of catastrophe, that is:

coronary vasodilation	→ constriction and spasm
thrombolytic	→ thrombotic
left ventricular compliance	→ stiffening
orderly rhythm	→ ectopy and arrhythmia

These influences are increased by the catecholamine and sympathetic neural consequences of hypocapnia, as well as by the left hemispheric mental operating mode of the patient (13).

Four important references are available for those interested in hyperventilation:

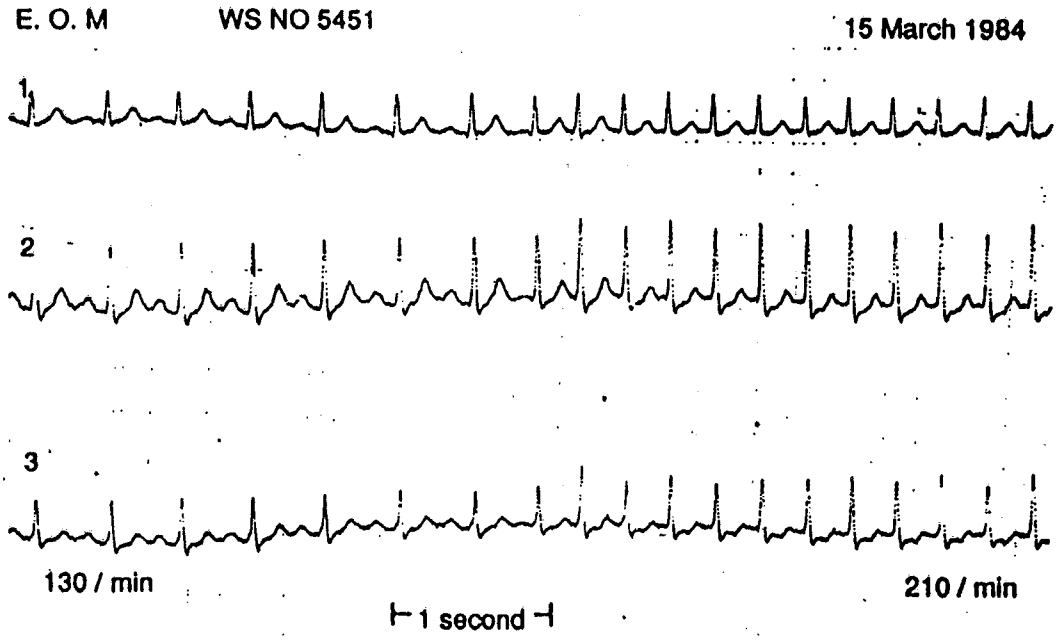

Figure 3. *Resting electrocardiogram in a white female dance teacher aged 21 years suffering from hyperventilation and anxiety (effort syndrome). The acceleration was related to an increase in hyperventilation when thinking about her lover's betrayal.*

Ayres and Grace's study of inappropriate ventilation as a cause of cardiac arrhythmia (19), the examination of delayed myocardial ischemia induced by anger (20), the biobehavioral background to sudden cardiac death (21), and a paper by Rozanski et al on the ability of personally relevant mental stressors to precipitate myocardial ischemia (22). It is my opinion that the combination of emotional arousal and hyperventilation is the major pathway by which the individual's perception of problems and emotional responses can damage the heart and destabilize the circulation. In the "think" test described below, anger is the most common stimulus to hypocapnia, which suggests that many individuals use hyperventilation subconsciously as a displacement activity for anger and frustration.

Excellent examples of alpha-adrenergic coronary constriction (23) and localized spasm (24) have been published. Spasm can be provoked by ergonovine and histamine injections, cold pressor stimulation, exercise, and isometric effort; however, the sixth agent, hyperventilation (25), is the most common cause met in practice. In following patients with hyperventilation-related heart disorders over the years, I have seen the development of localized coronary stenoses, concurring with the view (24) that stenosis can be created by spasm-induced intimal damage as well as by atheroma. I have put forward the view that vein grafts are more easily closed by hyperventilation than are the thicker native arteries they replace at operation and I believe that recurrence of stenosis after angioplasty is commonly due to untreated hyperventilation (Fig. 5).

DETECTION OF HYPERVENTILATION: WHEN TO CONSIDER IT AND WHERE TO LOOK

Hyperventilation should be suspected when ability and performance deteriorate and arousal increases. As the individual

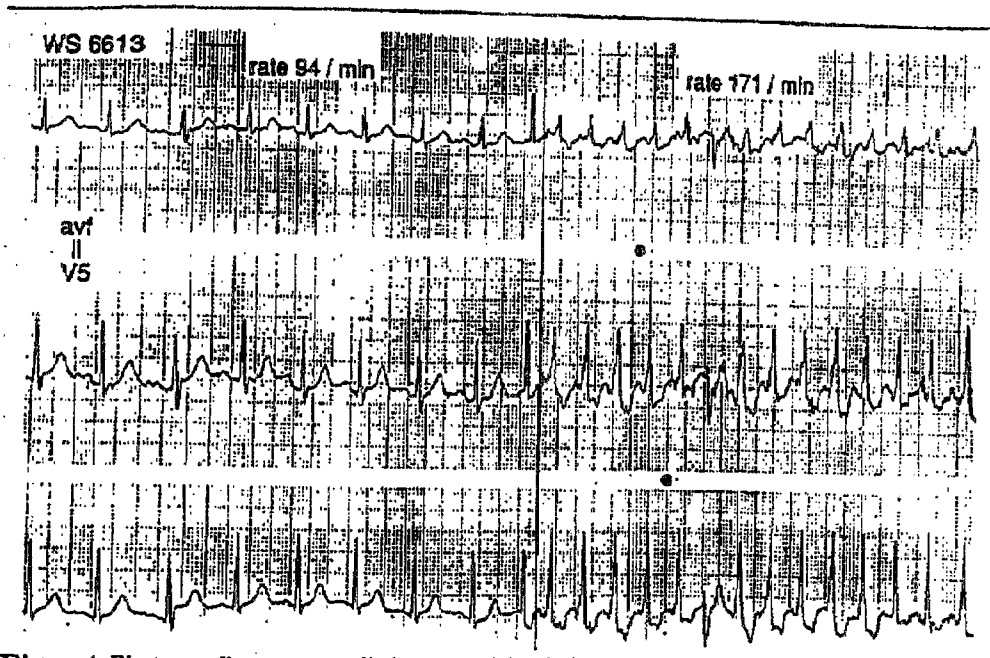

Figure 4. *Electrocardiogram at rest (94 beats per min) and after exercise stress testing (171 beats per min) in an unfit middle-aged hyperventilator. The result had been deemed positive for ischemia but there had been no coronary illness or event and the coronary arteriogram was normal. This type of error is usually avoided by monitoring partial pressure of carbon dioxide (pCO_2) during exercise.*

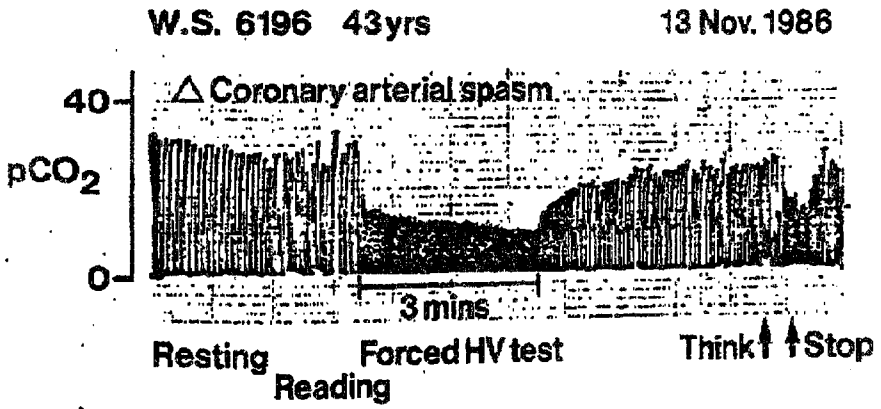

Figure 5. *Partial pressure of carbon dioxide (pCO_2) monitored in a patient with recurrent coronary arterial spasm. The tracing represents the pCO_2 in the air drawn through a fine tube from the dominant nostril. The resting end-tidal level is borderline at the start (32 mm Hg) and falls into frank hypocapnia (26 mm Hg) before reading aloud. At three minutes from the end of the forced hyperventilation (HV) test the level is still 26 mm Hg. On the patient being invited to think about his predicament, there is a swift fall to 15 mm Hg, recreating the risk of further spasm.*

TABLE I

CATABOLIC AND ANABOLIC PROCESSES

Hormonal Pattern during Arousal

Catabolic Hormones Increase	Anabolic Hormones Decrease
Cortisol	Insulin
Epinephrine	Calcitonin
Glucagon	Testosterone
Growth hormone	Estrogen
Antidiuretic hormone	Prolactin
Renin	Luteinizing hormone
Angiotensin	Follicle-stimulating hormone
Aldosterone	Gonadotropin-releasing hormone (GnRH)
Erythropoietin	Prolactin-releasing hormone (PRH)
Thyroxin	
Parathormone	
Melatonin	

Anabolic and Catabolic States

Anabolic state

Increased synthesis of protein, fat, carbohydrate (growth, energy storage)
Decreased breakdown of protein, fat, carbohydrate (growth, energy storage)
Increased production of cells for immune system (white blood cells of thymus and bone marrow)
Increased bone repair and growth
Increase in sexual processes (cellular, hormonal, psychological)

Catabolic state (arousal)

Halt in synthesis of protein, fat, carbohydrate
Increased breakdown of protein, fat, carbohydrate (energy mobilization)
Elevated blood levels of glucose, free fatty acids, low-density lipoprotein, cholesterol (for energy)
Increased production of red blood cells and liver enzymes (for energy)
Decreased repair and replacement of bone
Decreased repair and replacement of cells with normally high turnover (gut, skin, etc.)
Decreased production of cells for immune system (thymus shrinks, circulating white cells decrease)
Decreased sexual processes
Increased blood pressure, cardiac output
Increased salt and water retention

(Reproduced, with permission, from Sterling P, Eyer J *Soc Sci Med* 15E: 3-42, 1981)

Hyperventilation

IN BRIEF

Chronicity alters the clinical presentation of hyperventilation. Muscular aches and pains and influenza-like symptoms become more prominent than the cardiovascular symptoms, possibly because adrenal cortical activity wanes while adrenal medullary influence wanes. Misdiagnoses (e.g., Epstein-Barr virus, post-viral fatigue syndrome, myalgic encephalomyelitis) are often made by physicians who are unfamiliar with the chemical and metabolic changes of chronic hyperventilation.

moves over the top of the performance-arousal curve there is a shift from stability toward instability (Fig. 3). Hyperventilation generates or amplifies arousal mechanisms and promotes catabolic degradation. Hyperventilation should be considered in effort syndrome, Da Costa's syndrome, mitral prolapse, anxiety states, panic attacks, phobias, burnout, and posttraumatic stress disorders, and among patients "who have never been the same" since an event or accident "changed the course of their lives."

It is not rare to encounter a hyperventilation-induced cardiovascular catastrophe such as myocardial infarction from coronary spasm some months after a bereavement, loss of job, motor accident, industrial injury, admission to a coronary unit, or some other incident that carried the individual beyond the limits of physiological tolerance. One should consider hyperventilation when blood pressure, sugar, lipids, uric acid, and coagulability reach abnormally high states for the individual, or when an exhausted individual has multisystem symptoms fitting the patterns of disorder described by Lum (16) and Magarian (17).

Hyperventilation increases calcium ionization in smooth-muscle cells and can, therefore, initiate the crucial physiological disturbances in migraine, transient disorders of cerebral blood flow, cerebral vasospasm, asthma, coronary spasm, duodenal spasm with creation of a hiatus hernia, spastic colon and irritable bowel syndrome, and genitourinary disturbances. I have seen hyperventilation induce laryngeal spasm, premature ejaculation, renal colic, and fail-

ure of transurethral resection of the prostate.

• *In the Undiseased Cardiovascular System.* Hyperventilation associated with a high arousal state is probably the major mechanism of angina pectoris, positive exercise stress tests, myocardial ischemia and infarction, and sudden coronary death when the atheromatous element of disease is absent or too slight to cause the coronary catastrophe (2). Chest pain associated with loss of capacity for making and sustaining effort is commonplace (26). An episode of chest pain with electrocardiographic (ECG) abnormalities and left ventricular dyskinesis but a normal coronary arterial appearance is virtually diagnostic of an episode of coronary vasospasm. Fast cardiac arrhythmias initiated by hyperventilation mechanisms include supraventricular tachycardia with normal conducting systems and the Wolff-Parkinson-White syndrome. Rosenbaum's right ventricular ectopy is common among hyperventilators, and its appearance in a coronary-care unit should lead to an examination of the blood gases for hypocapnia and alkalosis in the likelihood that cardiac depressant drugs for suppression can be avoided.

Hyperventilation can cause severe arterial constriction. The victims may present with Raynaud's disease or arterial insufficiency of the foot, or with raised blood pressure when the increased force of cardiac contraction forces blood into a constricted arterial bed.

Exercise stress testing should not be performed without end-tidal partial pressure of carbon dioxide (pCO_2) monitoring because the incidence of false-positive tests is high among hyperventilators and leads to an extravagant overuse of coronary arteriography (Fig. 4).

• *In Organic Heart Disease.* One should consider vasoconstrictive and vasospastic influences of hyperventilation whenever the amount of effort required to stimulate angina pectoris varies widely from one day to another, when it is strongly influenced by fatigue and emotional upset, and when it is subject to diurnal variation (2,27). In organic coronary arterial disease, hyperventilation can produce common accompaniments of angina pectoris (e.g., alterations of consciousness, angor animi, or panic) by altering cerebral blood flow. By dulling the perception of pain it can produce silent ischemia. Hyperventilation is an adequate cause of the arm pains, numbness, and paresthesias that are commonly associated with coronary heart disease by laypersons, and of the aerophagia that causes pressure to be built up in the chest and relieved by belching. The sensations of airlessness and inability to take in a satisfying breath are characteristic of hyperventilation (27).

Wakening at 3 to 4 A.M. with angina pectoris can be part of the chronic hyperventilation syndrome in persons with organic coronary disease.

Closure of coronary arterial bypass grafts is one consequence of hyperventilation. They are probably more vulnerable to obliteration by spasm than are the thicker-walled native vessels. Angioplasty is probably doomed to fail if the patient is not taught to avoid hyperventilating under conditions of exhaustion and strain.

Myocardial infarction occurring unexpectedly in a person with good exercise tolerance suggests the influence of hyperventilation, which can produce this catastrophe by cracking a plaque and inducing thrombotic occlusion or by damaging the intima of the artery and provoking obliterative thrombosis. I always think of spasm from hyperventilation when I see short segments occluded or narrowed in a person with an otherwise healthy coronary arteriogram, or hear the history of genuine angina pectoris

IN BRIEF

Cardiovascular changes are induced by hyperventilation. Their influence is to shift vital equilibria in the direction of catastrophe, that is, coronary vasodilation to constriction and spasm, thrombolytic to thrombotic, left ventricular compliance to stiffening, and orderly rhythm to ectopy and arrhythmia. These influences are increased by the catecholamine and sympathetic neural consequences of hypocapnia, as well as by the left hemispheric mental operating mode of the patient.

cropping up for short periods at times of strain in an otherwise healthy individual.

Easily reversible cardiac arrest and sudden coronary death with little atheromatous disease is extremely suggestive that hypocapnic mechanisms have been influential.

Atherosclerotic coronary disease is a handicap that increases the risk of occlusion from spasm.

CLINICAL EXAMINATION AND TESTING

Hysterical hyperpnea is not a part of cardiological practice. The overbreathing that produces cardiovascular disturbances can be rapid and arrhythmic and associated with prominent upper chest movement and sighing, but usually it is unobtrusive and passed as normal during the consultation. Okel and Hurst explained that the ventilation required to maintain hypocapnia is much less than the overbreathing needed to induce it (28).

During the interview, it is important to pay attention not only to what the patient has to say but also to the way in which the verbal message is delivered; changes in breathing can give a clue to highly charged emotional stimuli and personally relevant stressors that words deny. A mindless repetition of questions without assimilation of answers and increasingly disordered breathing may indicate that the patient feels trapped, incapable of coping with problems, but too exhausted to take in the answers given by the doctor (29). Grossman and de Swart's questionnaire can be useful (30).

The physician looks for clues of chronic hyperventilation in the history (e.g., the wakening with symptoms at 3 to 4 A.M. and the inability to relax after effort).

In acute cardiovascular illnesses, particularly in arrhythmias and acute myocardial ischemia, it is extremely important to consider hyperventilation; its influence might be dominant and overwhelming. Nothing provides such a shock to the unwary in the emergency room as the demonstration of gross hypocapnia and alkalosis in a case hitherto refractory to treatment. Blood-gas analysis should always be available.

IN BRIEF

Hysterical hyperpnea is not a part of cardiological practice. The overbreathing that produces cardiovascular disturbances can be rapid and arrhythmic and associated with prominent upper chest movement and sighing, but usually it is unobtrusive and passed as normal during consultation. The reason for this is that the ventilation required to maintain hypocapnia is much less than the overbreathing needed to induce it.

The most common diagnostic problem of hyperventilation in cardiology is to decide whether hypocapnia is the cause of episodic disorder. Asking the patient to overbreathe in the hope that the symptoms might be reproduced in the office or at the bedside usually is a waste of time because the range of arousal experienced sitting there is qualitatively and quantitatively different from that experienced when the disorders occurred.

The infrared mass spectrophotometer (4), or capnograph, can be used continuously to monitor the pCO_2 content of the expired air drawn through a fine plastic tube from the dominant nostril. The end-tidal carbon dioxide ($PetCO_2$) level is close to the arterial value when the lung function is normal. In routine practice (Fig. 5), we record the resting level and carry out a forced hyperventilation test. (By unofficial international agreement, this used to last for three minutes [31]; now, however, many workers settle for a one-minute hyperventilation challange.)

At the end of this test, the patient is asked to close his or her eyes and to think about emotionally charged stimuli or personally relevant stressors. These are usually detected by alterations of breathing during the history taking. Thoughts of anger and helplessness can be particularly provocative of hypocapnia. The capnograph can be used to plot steadily falling and fluctuant pCO_2 levels, and the breath-holding attacks found when abreaction follows the request to think about emotionally charged stimuli. The pCO_2 level can also be followed as the patient is asked to recall symptoms or mimic

the breathing patterns he or she associates with them. Inviting the patient to "psyche up" as for effort or aggression can produce a dramatic effect in some who use the adrenergic drive of hyperventilation to prepare themselves for activity or opposition.

It is appropriate to use the capnograph during exercise stress testing. In hyperventilation disorders, the limits of effort can be imposed by hypocapnia irrespective of the presence of organic coronary disease, and the hypocapnia can be accompanied by the ECG appearances of ischemia even when the coronary arteriogram is normal (Fig. 4).

The management of hyperventilation-related disorders is not described in this article, but the paper by King (29) is recommended.

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