

Hyperventilation Syndrome

A Clinical and Physiological Evaluation

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MOST PHYSICIANS are quite familiar with the isolated attack of acute hyperventilation that is characterized by dramatic overbreathing and classically culminates in tetany. Although terrifying to the patient, and almost equally alarming to any on-looker, these attacks are usually brief and without serious medical sequelae. Recently we have come to recognize a chronic hyperventilation pattern that appears to be far more common, far more disabling but, paradoxically, less well known than the acute variety.^{5,6,7,8} This report will present an analysis of 250 patients with hyperventilation syndromes and will emphasize the clinical characteristics and course of this chronic hyperventilation pattern.

As Table 1 indicates hyperventilation was psychogenic in origin in about 70 per cent of the patients in this series, with almost three times as many women as men falling in this category. There was an organic basis in only 2 per cent of the cases, usually infections and/or intoxications of the central nervous system.^{1,10} In the remaining 28 per cent, designated as "mixed," organic and psychological factors were jointly responsible. In these two latter groups the sexes were about equally involved.

There are symptoms and signs referable to most body systems as a consequence of the diffuse biochemical and physiological changes resulting from overbreathing. The most prominent of the clinical features are listed in Table 2. Out of this welter of alarming bodily sensations the patients usually tend to focus on but a few, most often on symptoms referable to the cardiovascular or nervous system, and become exceedingly fearful that they are experiencing either a "heart attack" or a "stroke." An analysis of the chief or presenting complaints (see Table 1) reveals that over one half of the patients had concentrated on cardiovascular symptoms, and another one fifth on neurological symptoms, to the relative exclusion of the many other bodily changes that had occurred at the same time. Curiously, respiratory symptoms were not particularly prominent although changes in respiratory behavior were usually evident to any observer.

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• There is a chronic hyperventilation syndrome which is much more common, of greater medical significance and far more difficult to diagnose than the better-known acute hyperventilation attack. This chronic syndrome tends to mimic grave organic disease with which it frequently is associated or superimposed.

Studies on 250 patients with chronic hyperventilation patterns revealed the rapidity with which biochemical and physiological changes can occur and the characteristics of the resultant symptoms and signs, with particular reference to the heart and lungs.

Once the diagnosis is suspected and appropriately confirmed, it is possible to "cure" over 70 per cent of such patients by means of simple therapeutic measures.

With hyperventilation there is a rapid fall in arterial carbon dioxide tension ($p\text{CO}_2$) and rise in pH and, in turn, a reduction in cerebral blood flow and in the frequency of the brain waves. When the brain waves slow to 5 cycles per second or less some disturbance of conscious awareness usually results, ranging all the way from simple faintness to complete loss of consciousness.³ There is a concurrent increase in neuromuscular irritability, likely related to rapid changes in serum potassium and ionized calcium concentration that are believed to occur with these abrupt shifts in arterial carbon dioxide tension and pH.⁸ These are the factors that underlie the peripheral and circumoral paresthesias so characteristic of this syndrome, and the accompanying muscular tremors, spasms and aches. Occasionally, and presumably as the result of hysterical mechanisms, these peripheral paresthesias and myalgias are asymmetrical and may even be unilateral.^{6,8} These central and peripheral neurological phenomena are extremely alarming to the patient, who fears he is either "losing his mind" or on the verge of a "stroke."

By direct action on the blood vessel wall, the rapid reduction in arterial carbon dioxide tension decreases the peripheral vascular resistance and thus lowers the arterial blood pressure.² This and the associated shift in electrolyte and acid-base balance, bear importantly on the impressive tachycardia, frequent arrhythmia and perplexing electrocardiographic changes that commonly occur with hyper-

TABLE 1.—Clinical Data on 250 Patients with Hyperventilation Syndrome

Pathogenesis	No. of Patients	Sex		Presenting Syndrome					
		M	F	CV	GI	N	MS	R	Gen
Psychogenic	176	49	127	88	8	39	8	11	22
"Mixed"	69	31	38	42	1	10	6	5	5
Organic	5	3	2	4	1
Total	250	83	167	130	9	53	15	16	27

CV = Cardiovascular; GI = Gastrointestinal; N = Neurological; MS = Musculoskeletal; R = Respiratory; Gen = General.

ventilation.^{7,8,11} Precordial pain, in the form of recurring sharp twinges or a more prolonged dull discomfort, is another prominent feature of this syndrome and has been correlated on various occasions with the onset of cardiac arrhythmia,⁴ spasm of the diaphragm,¹² prolonged intercostal muscle spasm and gastric distention.⁸

To the patient these symptoms often suggest serious heart disease and, as our experience has indicated, the physician is too frequently misled as well, particularly when confronted by objective changes in the heart rate, rhythm and electrocardiogram.

Patients with the chronic hyperventilation syndrome present clinical pictures of variable duration and intensity which in general may resemble many chronic illnesses. At first glance the clinical features may seem non-specific; often they will suggest a psychogenic process. It is with the "mixed" cases in particular that sins of omission or commission are likely to occur. Too often the total illness is ascribed to *either* the organic *or* the psychogenic component. The inevitable result here is inadequate and improper treatment, usually with prolonged disability and occasionally with more serious consequences.

DIAGNOSTIC CLUES

The course of the chronic hyperventilation pattern tends to be interrupted periodically by recurring acute exacerbations that resemble in many ways the acute syndrome. These acute exacerbations mainly occur during the day and rarely if ever will awaken a person from a sound sleep. Patients may comment at first on nocturnal attacks, but inquiry usually will elicit that symptoms began at times the patient was partially awake such as soon after retiring or just before fully waking in the morning.

These acute exacerbations are not clearly correlated with physical exertion even though, on initial questioning, the patients may so suggest. Close checking will usually reveal that the symptoms began *after* rather than *during* exertion, often at the end of a tiring, tension-filled day.

Another feature, briefly mentioned earlier, is the patient's curious lack of awareness of his over-breathing or, when he is aware of it, his usual

TABLE 2.—Multisystem Involvement in Hyperventilation Mechanisms

1. **NEUROLOGICAL:**
 - A. Central: Disturbances of Consciousness—Faintness, dizziness, unsteadiness, impairment of concentration and memory, feelings of unreality, "losing mind," complete loss of consciousness (infrequent)
 - B. Peripheral: Paresthesias: Numbness, tingling and coldness of fingers, face and feet
2. **MUSCULOSKELETAL:** Diffuse and/or localized myalgia and arthralgia, tremors and coarse twitching movements, carpedal spasm and generalized tetany (infrequent)
3. **RESPIRATORY:** Cough, chronic throat "tickle," shortness of breath, atypical "asthma," tightness in or about the chest, sighing respiration, excessive yawning
4. **CARDIOVASCULAR:** Palpitations, "skipped beats," tachycardia, atypical chest pains—sharp precordial twinges, dull precordial or lower costal ache—variable features of vasomotor instability
5. **GASTROINTESTINAL:** Oral dryness, globus, dysphagia, left upper quadrant or epigastric distress, aerophagia, belching, bloating and flatulence
6. **PSYCHIC:** Variable anxiety, tension and apprehension, inappropriate pseudocalmness (hysterical subjects)
7. **GENERAL:** Easy fatigability, generalized weakness, irritability and chronic exhaustion, frightening dreams, sleep disturbances

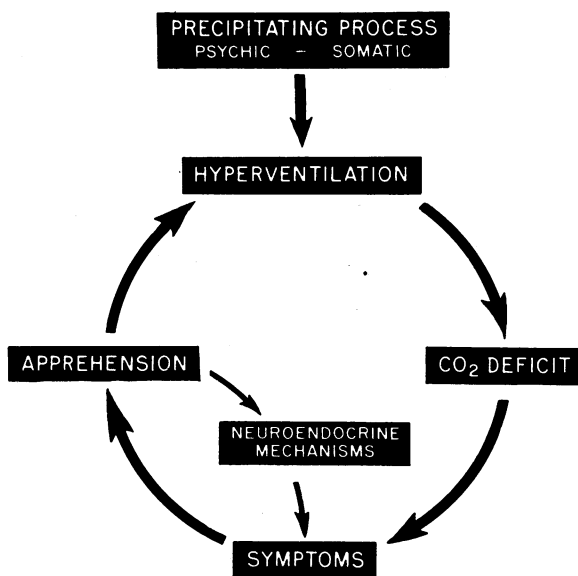


Chart 1.—Sequence of events characterizing hyperventilation syndrome.

insistence that it was a *result* of the attack and did not develop until *after* the episode was well under way. The basis of this belief and a schematic representation of the sequence of events that characterizes the hyperventilation syndrome is presented in Chart 1.

Whatever the nature of the precipitating process,

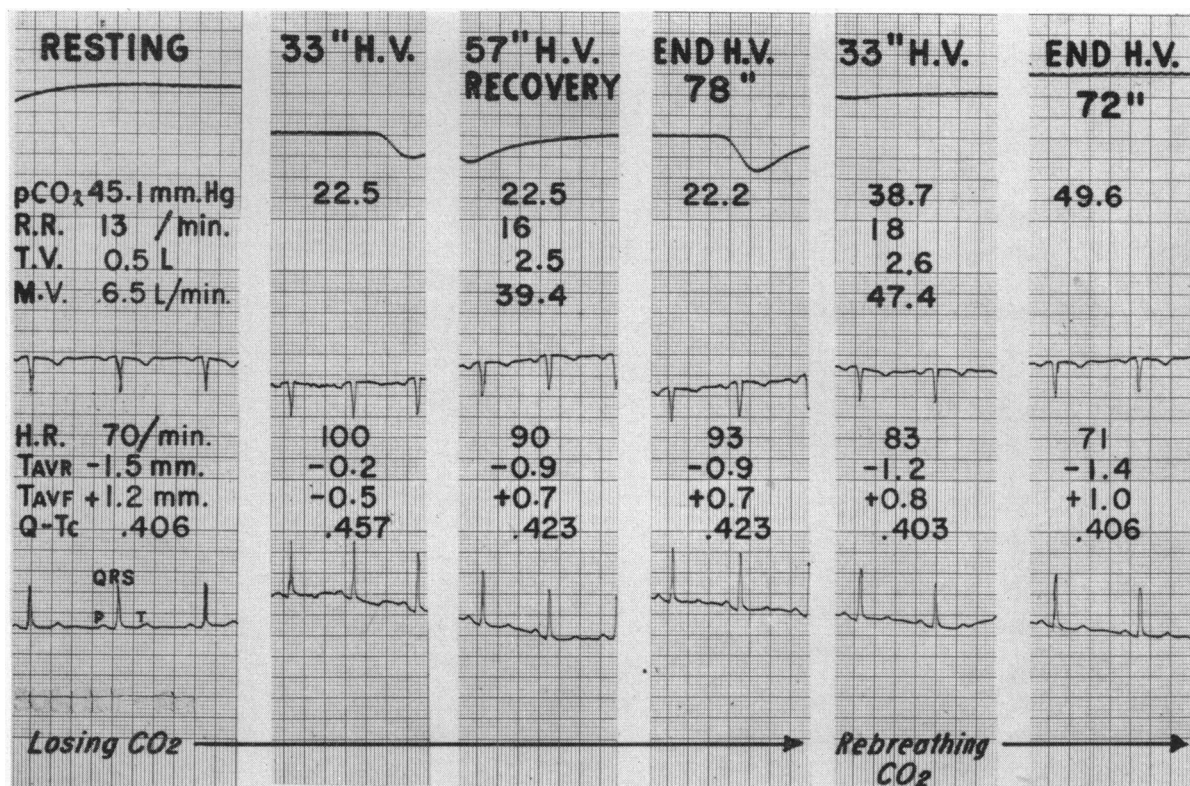


Figure 1.—Representative sections from record of normal subject during standard H.V. experiment. H.V. with rapid reduction in pCO₂ (viz. "Losing CO₂") results here in maximum electrocardiographic changes at 33 seconds and then, despite maintained H.V. and low pCO₂, in return of cardiac indices toward normal at 57 seconds ("recovery"). When pCO₂ not reduced (viz. "Rebreathing CO₂") no significant cardiac phenomena occur. (See text for more detailed discussion.)

Abbreviations: H.V. = Hyperventilation; R.R. = Respiratory rate; H.R. = Heart rate; pCO₂ = Carbon dioxide tension; T.V. = Tidal volume; M.V. = Minute volume; QTc = QT interval corrected for heart rate.

the initial link in the pathogenetic chain is the overbreathing. This results in a reduction in arterial carbon dioxide tension and a concurrent rise in pH. Critical changes in these indices can be achieved in the first 30 seconds of hyperventilation even though a further 60 to 90 seconds may be needed for maximal changes.⁸ These primary changes appear to initiate the widespread biochemical and physiological phenomena that follow and are responsible for the multiple clinical manifestations. It is our impression that up till this point most patients are preoccupied with various disturbing details related to the precipitating process and thus are not at all aware of their respiratory aberrations. It is only when the intermediate mechanisms have been called into play that the alarming symptoms develop and intrude into their conscious awareness. Then, for the first time, they may notice their rapid, labored breathing and thus come to insist that their respiratory changes followed rather than preceded the onset of their acute attacks. Patients are usually terrified by the unexpected impact of these alarming symptoms, and their fear, as depicted in Chart 1, tends to accentuate and prolong the overbreathing and

simultaneously, we suspect, to bring about endocrine and autonomic nervous system responses. This is the inner neuroendocrine pathway noted on the diagram, which, as will be described later, often contributes importantly to the total cyclic process.

LABORATORY STUDIES

Detailed presentation of the cardiac, pulmonary and acid-base balance data obtained during our hyperventilation studies already has been reported.^{7,8} In brief, we studied a group of normal subjects and a group of "chronic hyperventilators" during two similar periods of voluntary overbreathing in an identical laboratory setting. The subjects were placed in a closed breathing system that included an infrared carbon dioxide analyzer to provide us with a rapid and continuous record of the changing alveolar carbon dioxide tension which, for all practical purposes, is identical to the arterial carbon dioxide tension. We obtained continuous spirometric and electrocardiographic data at the same time and, in certain subjects at suitable intervals, we drew femoral arterial blood for pH determination. During

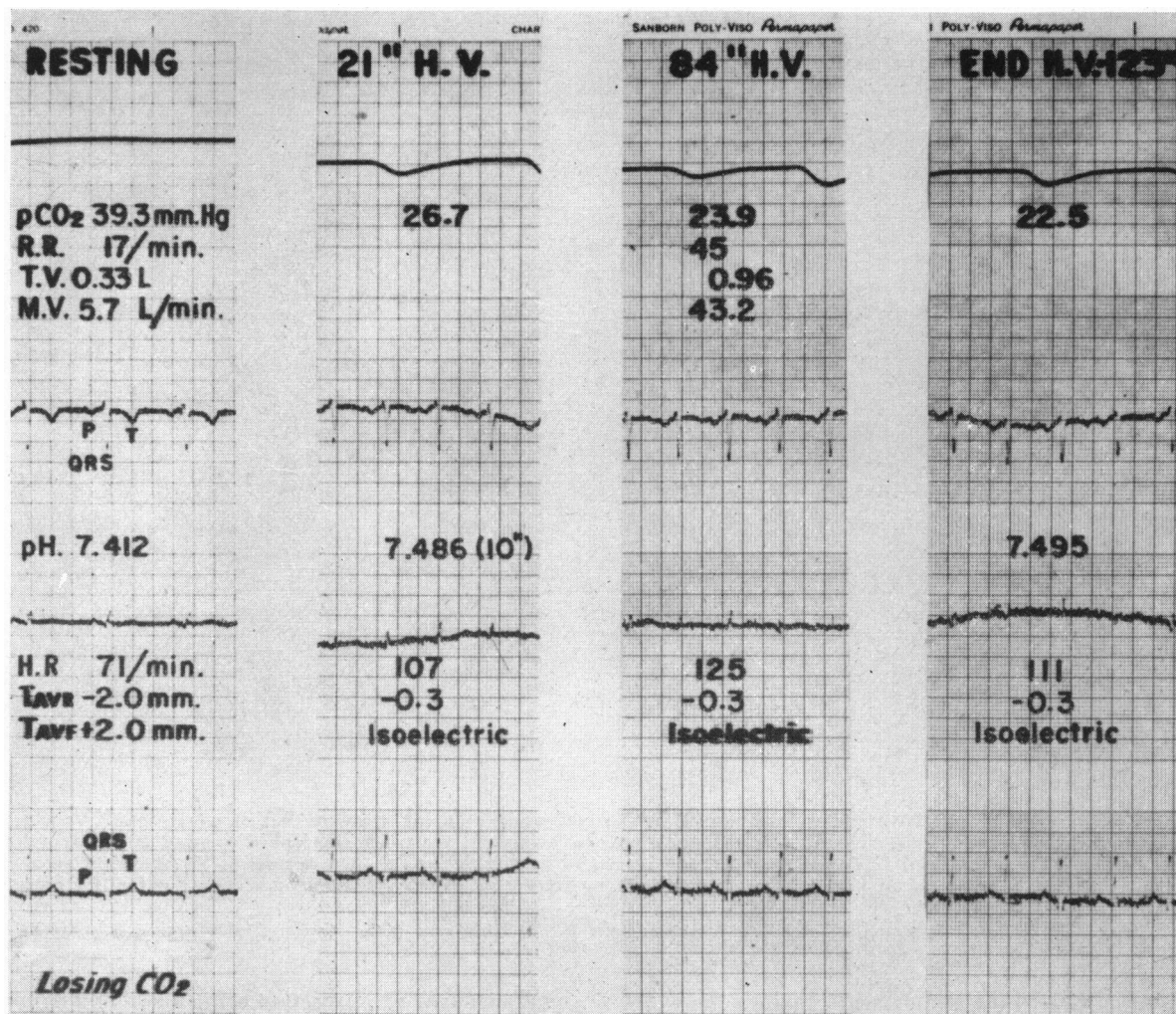


Figure 2.—Representative sections from record of "hyperventilator" during standard H.V. experiment when pCO₂ abruptly reduced. Typical electrocardiographic changes in H.R. and T waves occur in 21 seconds and the arterial pH rises impressively within 10 seconds. No evidence of cardiac "recovery" is seen. (See text for more detailed discussion.)

Abbreviations: H.V. = Hyperventilation; R.R. = Respiratory rate; H.R. = Heart rate; pCO₂ = Carbon dioxide tension; T.V. = Tidal volume; M.V. = Minute volume.

one period of voluntary hyperventilation a canister of soda lime was introduced into this closed respiratory system which absorbed the expired carbon dioxide and expedited the drop in alveolar carbon dioxide tension. This canister was absent during the second period of overbreathing so the subject was able to rebreathe his expired gases, thus inducing a progressive rise in alveolar carbon dioxide tension. These two periods of hyperventilation were therefore identical except for the opposing changes in alveolar carbon dioxide tension.

Figure 1 shows representative sections from the continuous record of a typical experiment on a normal subject. The section on the far left presents the resting or control data. The upper sloping horizontal line represents the alveolar carbon dioxide tension, which in this case was 45 mm. Hg. Below this are noted the respiratory rate, tidal and minute

volumes and pertinent electrocardiographic data. Moving from left to right the next three sections illustrate the cardiopulmonary changes occurring during acute hyperventilation (in the presence of the canister of soda lime). The carbon dioxide tension at 33 seconds confirms the rapidity with which such reductions can be achieved. Little further reduction occurred after 78 seconds of overbreathing. The mean respiratory data for the entire period noted in the 57-second section confirm the increased pulmonary ventilation that occurred.

The electrocardiographic tracings show that at 33 seconds the heart rate increased from 70 to 100 beats per minute; the T_{AVR} was almost isoelectric at that time and the T_{AVF} had been converted from a positive deflection of 1.2 mm. to a negative deflection of 0.5 mm.; and the Q-Tc had lengthened to 0.457. (The accepted upper limit of normal for the

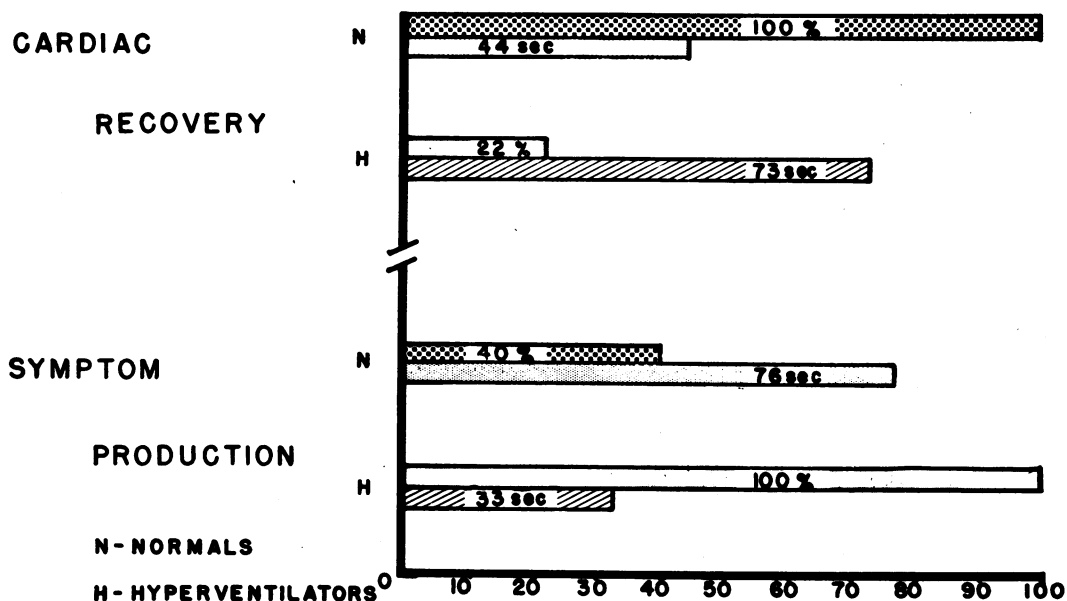


Chart 2.—Response patterns to voluntary hyperventilation. Upper section of chart shows that all normals (N) achieved partial or complete electrocardiographic “recovery” during H.V. at mean time of 44 seconds in contrast with 22 per cent of “hyperventilators” (H) who required mean time of 73 seconds. Lower section of chart shows that typical H.V. symptoms developed in all “hyperventilators” early (mean time 33 seconds), whereas only 40 per cent of normals had mild symptoms and these occurred much later (mean time 76 seconds).

Q-Tc is 0.425.) This increase is indicative of an abnormal prolongation of electric systole at the expense of diastole, which is the reverse of what one would normally expect with an acceleration in heart rate.

It is evident that at 57 seconds of hyperventilation, despite the continued overbreathing and reduced alveolar carbon dioxide tension, the tachycardia was decreasing, the T-wave changes were reverting and the Q-Tc had returned to just within normal range. These phenomena were regarded as indicative of “cardiac recovery” on the assumption that some degree of cardiovascular compensation for the reduced carbon dioxide tension had been achieved. These “recovery” phenomena persisted to the end of the hyperventilation period even though the alveolar carbon dioxide tension diminished a little more.

The two final sections on the right represent comparable stages of the second period of hyperventilation when, with the soda lime canister absent, the subject rebreathed his own expired gases which slowly increased the alveolar carbon dioxide tension. In these two sections, despite an even greater respiratory exchange than during the first period, no significant electrocardiographic changes occurred.

This sequence of events was typical of all the normal subjects, which tends to confirm the thesis that it is the rapid fall in arterial carbon dioxide tension that induces these electrocardiographic phenomena, rather than the increased ventilation or

heart rate per se or the changes in position of the heart and/or the diaphragm.

When the patients with chronic hyperventilation were put through the same experimental procedures, they had similar and often more striking electrocardiographic changes but in them there was virtually no evidence of the “cardiac recovery” phenomena. This apparent inability to compensate electrocardiographically is clearly demonstrated in Figure 2, which demonstrates as well the rapidity with which significant changes in arterial pH can occur in a person who hyperventilates. The pH rose from 7.412 at rest to 7.486 in 10 seconds of overbreathing and increased more slowly thereafter to 7.495 at 123 seconds. This illustrates the degree of respiratory alkalosis that can occur with even brief hyperventilation.

The bar graphs in the upper half of Chart 2 show that in all the normal subjects the “cardiac recovery” phenomena occurred, the mean time for the group being 44 seconds. Only 22 per cent of the “hyperventilators” showed a mild tendency in this direction, and in them it occurred at an average time of 73 seconds. The majority lacked any capacity to adjust or compensate in this way. The lower bar graphs indicate that 40 per cent of the normal subjects developed characteristic but rather mild hyperventilation symptoms after a mean time of 76 seconds of overbreathing. The hyperventilators on the other hand all developed symptoms that were quite severe and began on the average at 33 seconds.

The significance of these data is far from clear.

Our current impression is that the hyperventilators have become "conditioned" in a sense, so that they are able to reduce their carbon dioxide tension extremely rapidly. Paradoxically, however, they do not seem able to handle effectively the physiological sequelae of these abrupt variations of arterial carbon dioxide tension.

DIAGNOSIS

Although the acute hyperventilation syndrome is well known, the more common chronic pattern, with its insidious onset and tendency to simulate serious organic disease, is not well enough appreciated. Diagnostic and therapeutic errors are thus quite common. In only one of the first 150 patients in the present series with the chronic syndrome was the possibility of a hyperventilation mechanism suspected.⁸

In attempting earlier to describe the clinical features, I emphasized various characteristics that might serve as diagnostic clues. It should be clearly stated, however, that these particular characteristics are not always immediately apparent and often have to be carefully elicited from the many symptoms in the background that may be considered by the patient as relatively minor.

When one suspects the presence of a hyperventilation mechanism the diagnosis must be confirmed by reproducing a typical acute exacerbation with voluntary overbreathing. Persons who hyperventilate will have classic exhibition of their characteristic symptoms within the first 60 seconds of overbreathing, although a full-fledged attack may take a little longer. A minimum of 2 and preferably 3 minutes of overbreathing must be performed before a test can be considered negative. Should characteristic symptoms be reproduced, a medium (6 pound) paper sack is placed firmly over the patient's nose and mouth and he is requested to breathe slowly from it. This expedites the prompt elevation of the arterial carbon dioxide tension, and the patient's symptoms begin to subside within 30 to 60 seconds. He is permitted to remove the paper sack when he feels comfortable, and usually he does so voluntarily within 2 to 3 minutes. Occasionally patients who have demonstrated a decided secondary response pattern of apprehension may fail to react when voluntarily overbreathing in the reassuring environment of the physician's office. In such situations I have found it necessary to set the psychological stage before attempting to reproduce a typical acute attack.

THERAPY

Excluding the relatively few patients with an organic basis for their hyperventilation syndrome, the initial therapeutic step, when such a pattern is

suspected, is to attempt to reproduce the characteristic symptoms with voluntary overbreathing. When successful this both alarms and impresses the patient, and the rapid relief obtained with the paper sack is proportionately reassuring. This experience often evokes an emotional catharsis that in turn brings about temporary symptomatic relief while often shedding additional light on the nature of the underlying problems. This may provide the physician with valuable material for future discussion that would otherwise be unavailable to him.

In such cases, this experience is vital to the development of an effective physician-patient relationship. It demonstrates to the patient the reality of his symptoms on the one hand and at the same time reveals their emotional origin to him. With suitable explanation and reassurance he is able to appreciate the benign nature of the disorder, which helps to dispel his fears of serious disease and permits a more realistic approach to the basic problems. The average physician is quite capable of exploring and aiding in the solution of most of these problems.^{6,9} Apparent cure was brought about in approximately 70 per cent of the patients in the present series. Approximately 20 per cent achieved partial and/or temporary improvement, requiring periodic reassurance from time to time. The remaining 10 per cent were not helped and were found to be patients with severe depressive or hysterical patterns who needed prolonged psychiatric treatment.

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