

# The Hyperventilation Syndrome – Dr. Frances Ames



Dr. Frances Ames was a remarkable woman from South Africa. She was a neurologist, psychiatrist, and human rights activist. During her infancy in the early 1920s, her mother was abandoned by her husband and left penniless with three daughters. Despite this hardship, she achieved academic success and qualified as a doctor in 1942. In 1964, she was the first woman to be awarded an MD degree, medical doctor, at Cape Town University.

Ames was a proponent of the therapeutic benefits of cannabis, as she observed first-hand how cannabis relieved spasm in MS patients and helped paraplegics in the spinal injuries ward of her hospital. Her work is cited extensively throughout the cannabis literature.

When Nelson Mandela honored Dr. Ames with South Africa's highest civilian award, the Star of Africa, in 1999, he did so not for her achievements in the medical field but for the role she played in bringing to book the doctors who had acquiesced in the torture and death of the black activist Steve Biko.

In December 1952 she submitted the comprehensive thesis *The Hyperventilation Syndrome*, for the degree of Doctor of Medicine to the University of Cape Town.

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## CHAPTER 1 – INTRODUCTION

The hyperventilation syndrome is the name given to a distinctive group of symptoms and signs which are caused by an increase in the depth and rate of breathing. This abnormal breathing is nearly always the result of emotional stress.

The association between emotional stress and disorders of breathing is well-known: sighing with grief, gasping with rage, panting with fear, heaving with resentment. Of its origin, Darwin said, "Men, during numberless generations, have endeavored to escape from their enemies by headlong flight, or by violently struggling with them; and such great exertions will have caused the heart to beat rapidly, the breathing to be hurried, the chest to heave and the nostrils to be dilated.....And, now, whenever the emotion of fear is strongly felt, though it may not lead to any exertion, the same results tend to reappear through the force of inheritance and association."

Cannon (1920) described hyperventilation as a preparation for flight or fight:

*"The forced respirations in deeply emotional experiences can be interpreted, therefore, as an anticipatory reduction of the carbon- dioxide in the blood, a preparation for the augmented discharge of carbon- dioxide into the blood as soon as great muscular exertion begins."*

Primitive man could and did take to his heels or use his fists if afraid. Modern man, inhibited by cultural and social traditions of behavior, is unable to do so. So the age-old physiological preparation for flight or fight is not carried over into any functional motor activity. This is when trouble arises. A strong emotional reaction with no motor outlet turns on itself to cause a physical upset.

In this paper, a study is made of the symptoms and signs by which to recognize this syndrome, and of some of the physiological mechanisms which are brought into operation.

## CHAPTER 2 – HISTORICAL REVIEW

The first description of the effects of overbreathing in man appeared as a footnote to an article by Haldane and Poulton (1908), the physiologists. They used forced breathing on themselves during experiments on the effect of want of oxygen on respiration, and the footnote comments: "*Poulton, after about a minute of forced breathing, began to feel tingling in the hands and to a less extent in the feet. This became very painful, the pain reaching a maximum usually about half a minute after the apnoea had begun. The tingling was accompanied by numbness and sweating of the hands and a peculiar sense of giddiness and abnormality almost resembling the effects of anoxemia. Except for the feeling of abnormality these symptoms were absent in Haldane even after 5 minutes of forced breathing.*"

They mentioned that forced breathing had been used to produce partial anesthesia for slight operations and attributed the disturbance of consciousness to loss of carbon dioxide. "*Deficiency of*

*CO2 appears to produce a condition of diminished excitability, but the explanation of the tingling sensations is by no means clear.*" They were impressed by the apnoea following overbreathing and mentioned that Cingalese pearl divers hyperventilate before diving as a form of religious ceremony. Poulton demonstrated to the Physiological Society the effect on himself of forced breathing. During the period of apnoea *"some of those present thought that something was wrong with Poulton and could hardly be restrained from performing artificial respiration. One or two of them were so affected that they became faint or sick and had to retire hastily. The face gradually assumes the leaden corpse-like hue of great anoxemia and it may be about a minute after this change begins before any desire to breathe is experienced."*

Henderson (1909) made a study of the effects of overbreathing. He hyperventilated sixty subjects for 45-90 seconds and concluded that the effects were similar to those of shock. He, too, was impressed by the apnoea and warned that it might be a danger in prolonged overbreathing. He cited experiments on anesthetized dogs, where, he said, 25-30 minutes of artificial respiration led to apnoea so prolonged that the heart failed after 7-8 minutes from lack of oxygen. He considered that apnoea almost invariably followed overbreathing and found it absent in only two or *"possibly three"* of his sixty subjects. Symptoms following overbreathing were more severe in these people. There appears to have been a tacit assumption by all subsequent workers that the majority of subjects after overbreathing experience this cessation of breathing during which time the CO<sub>2</sub> of the alveolar air is built up again.

It was not until 1946 that Mills, describing the respiratory pattern after 1-1 1/2 minutes of overbreathing in thirty-five subjects selected at random, found that only ten of these showed apnoea fairly consistently after hyperventilation. Eight of his subjects continued to overbreathe, often with great vigor. The remaining 17 showed an intermediate picture. Mills could not find any obvious physiological reason for the hyperpnoea of eight of his subjects and concluded that *"it results directly from that same cortical activity which is initially responsible for the forced breathing."*

The circulatory derangements after overbreathing were again emphasized by Hill and Flack (1910). They found that *"polygraph tracings show acceleration and enfeeblement of the pulse during forced breathing; the pulse can be felt to become weak or even disappear with each inspiratory effort, to return with expiration. Systolic blood pressure falls considerably with each inspiration."* In 1928 Vincent and Thompson investigated blood pressure changes during overbreathing. They found that 90% of people showed an average fall of 25 mmHg in systolic pressure. The remainder showed an average rise of 37 mmHg. The only difference between the two groups was that the subjects whose blood pressure rose had very slow initial pulse rates.

In 1938 Soley and Shock made an interesting observation: *"We have been impressed by the peripheral vasoconstriction which is so marked during forced breathing that the fingers must be stabbed deeply to obtain blood for chemical studies."* Kety and Schmidt (1946) did continuous blood pressure readings and measured cardiac output in five volunteers. They found that the blood pressure did not fall, in fact, it tended to rise in some cases, though not significantly. Cardiac output was reduced 11% during passive hyperventilation, but during active hyperventilation, it was maintained by a constant tachycardia.

The neuromuscular effects of overbreathing were first noted by Vernon (1909). He had suggested that divers might remain underwater for 9-10 minutes by combining oxygen inhalation with hyperventilation and utilizing the subsequent apnoea. On trying it on himself he was struck by the fact that after 6 minutes of overbreathing his hands passed into a condition of tonic rigidity and for the first 1 1/2 minutes of the subsequent apnoea were *"completely paralyzed"*.

More than 10 years passed before the clinical importance of this observation was realized. Then Grant and Goldman (1920) recognized that many of the symptoms and signs following overbreathing corresponded with those of tetany. The fact was driven home to them in a dramatic fashion during an experiment with Goldman as the subject. Grant describes it thus: *"After breathing very deeply for 30 minutes A.G. suddenly went into a complete tetanic convulsion. At the onset, he involuntarily gave a loud high-pitched scream, probably due to the contraction of the muscles of respiration and the forcing of air out through contracted vocal cords. The entire body was rigid, all the muscles being contracted in tetanic spasm. The back was arched somewhat and all extremities extended completely. Relaxation occurred within 30 seconds, and there was no further spasm"*. They also noted, unlike Vernon, that the tetanic spasm could be overcome by an act of will and mentioned that this is also possible in the spasm of idiopathic tetany.

The next step was to explain the pathogenesis of this tetany of hyperventilation. Grant and Goldman thought that it was primarily due to an alkalosis in the body. The reduction of CO<sub>2</sub> in the alveoli by overbreathing caused a reduction of CO<sub>2</sub> in the blood. This disturbed the B<sub>2</sub>CO<sub>3</sub> : NaHCO<sub>3</sub> ratio and produced an alkalosis because CO<sub>2</sub> is washed out of the blood more rapidly by overventilation than NaHCO<sub>3</sub> is decreased by excretion or other means.

Although they considered the alkalosis to be of primary importance they also attempted to find a link with the familiar tetany of hypocalcemia. Serum calcium levels in their cases were normal so they suggested that when the *"CO<sub>2</sub> of the blood is reduced by overventilation, a portion of the calcium is in some way rendered inactive though still present in the circulating blood"*.

Estimation of serum calcium appeared as almost a routine investigation during experiments on hyperpnoea after this. The only workers who claimed a significant calcium change were Barnes and Greaves (1936), who found a diminished calcium level in the cerebrospinal fluid after overbreathing. Their work was promptly refuted the following year by McCance and Watchorn (1937), and independently by Cumings and Carmichael (1937). All subsequent workers agreed that the serum calcium level either remains unchanged during hyperventilation, (Schultzer and Lebel (1939), O'Donovan (1943), or shows a slight rise (Forweather, Davidson, and Ellis (1940). Forweather et al. reported a marked drop in phosphate levels in the blood immediately after overbreathing but this work has not been confirmed.

During the year that Grant and Goldman's article appeared, Collip and Backus (1920) were also occupied with the cause of the symptoms of overbreathing. They found that during hyperventilation the CO<sub>2</sub> tension of the alveolar air fell 44% and the CO<sub>2</sub> combining power of the venous blood fell 14.3%. They also noted that the acidity of the urine was markedly decreased, a diuresis occurred and the rate of elimination of phosphates was increased. They concluded that the development of definite tetany and *"muscle cramps"* in many subjects during hyperpnoea was due to an alkalosis of the tissue. Alkalosis is today a well-recognized cause of tetany and the tetany following hyperventilation is generally accepted as being due to an alkalosis produced by the *"washing out of carbon dioxide"* from the blood.

In 1922 Goldman made a further significant contribution by showing that some people hyperventilate involuntarily thus producing symptoms. He gave the credit for the first description of such a case to Barker and Sprunt (1922) who described involuntary overbreathing with tetany production in a patient convalescing from epidemic encephalitis.

The first of Goldman's eleven cases was a medical student who, during an attack of gall bladder colic, involuntarily hyperventilated and found that this lessened his pain. In subsequent attacks, he

deliberately overbreathed to achieve this analgesic effect. He diagnosed the cause of his ultimate tetany himself, as he had often seen Goldman demonstrate the effect of hyperventilation during lectures. Five cases were students who had become tetanic during a class fight and in them, Goldman attributed this to excessive hyperpnoea following the acidosis of violent exercise. Two cases had acute infections with upper respiratory tract symptoms and one case had abdominal distension and vomiting. The remaining two cases were hysterical and Goldman commented that *"some cases of hysterical pseudo tetany are undoubtedly real cases of tetany due to over respiration"*.

It was only several years later that it became clear that involuntary hyperventilation in otherwise healthy individuals was usually the result of emotional stress. In 1929 White and Hahn drew attention to the symptom of *"sighing dyspnoea"* and described it as a valuable indicator of nervous tension. In 1934 Baker describing several cases stressed the importance of *"sighing dyspnoea"* as a manifestation of emotional stress. The same year Maytum and Willius (1934) recognized sighing dyspnoea as a form of hyperventilation. The following year Christie (1935), describing neurotic respiratory patterns, claimed that patients with conversion hysteria characteristically complained of *"an inability to return air into the lungs so that in mild cases deep sighing respirations were characteristic while in severe cases a paroxysm of hyperventilation leading to hyperventilation tetany might occur"*.

In 1942 Silverberg emphasized the importance of careful history taking in patients complaining of dyspnoea because in this way the breathing difficulty resulting from emotional stress could be readily differentiated from that of organic disease. Although healthy, individuals occasionally hyperventilate because of heat – Bazett and Haldane (1921), Wingfield (1941) and Dibden (1949), or because of excessive overbreathing after exertion – Goldman (1922) and Dibden (1949), most people do so as a result of emotional stress.

The effects of hyperventilation on the neuromuscular system led Rosett (1924) to advocate overbreathing as a simple, harmless technique for unmasking central nervous system disease. He took the view that the main effect of hyperventilation was on the cerebral cortex. *"In disease of the cerebrum, the manifestations referable to the particular system involved become vastly exaggerated under hyperpnoea. In injury of the pyramidal system, so slight as to escape detection by ordinary means, definite signs and symptoms are observable. Every form of abnormal involuntary movement referable to a disorder of the striatal system becomes exaggerated to the greatest possible extent. Mental abnormalities assert themselves in pronounced abnormal behavior"*. Hyperventilation is still used nowadays in an attempt to render doubtful neurological signs, for example, an equivocal plantar response, more definite.

The individual susceptibility of people to the effects of hyperventilation was emphasized by McCance (1932). He reported the cases of two women who *"with scarcely noticeable overbreathing"* went into tetanic spasm. He could not find any cause for this phenomenon. In 1939 Schultzer and Lebel again drew attention to the *"hypersensitive type"* and in 1943 O'Donovan described these people as individuals who, breathing at the rate of 55 – 60 breaths a minute, develop tetany in less than 2 minutes or who experience such severe symptoms within 2 minutes as to prevent them from continuing overbreathing. O'Donovan was inclined to think that predisposition to alkalosis could be induced *"so that with each hyperventilation the nervous system becomes more easily excited and responds in an increasing degree until tetany appears with a relatively small stimulus"*. He claimed that in some cases this hypersensitivity could be abolished by vitamin or other hypercalcemia therapy.

The clinical concept of hyperventilation was extended by Kerr, Dalton, and Gliebe (1937) who introduced the term *"hyperventilation syndrome"* to cover the many symptoms which had been

observed in patients who overbreathed involuntarily. They recognized that emotional stress lay at the root of the syndrome in most cases and made the important point that patients seldom presented with tetanic spasms but commonly did so with rather vague ill-defined symptoms. There is a risk here, however, of widening the concept too much and obscuring the fact that hyperventilation involves definite mechanisms which set a limit to symptoms and signs. Kerr et al. seem to have identified the hyperventilation syndrome with the anxiety state. Significantly, the following year Soley and Shock (1938) attributed all the symptoms and signs of "*effort syndrome*" to hyperventilation.

In 1938 a useful contribution came from Fraser and Sargant who described twenty cases of "*hyperventilation fits*" and differentiated them from hysterical and epileptic seizures.

In 1940 Fowweather, Davidson and Ellis thought that there was much justification for the term hyperventilation syndrome. They sought to explain the wide variation in clinical symptoms and signs by a tissue alkalosis which manifested itself in tetany in those individuals whose voluntary musculature was particularly susceptible, or in "*effort syndrome*" in those whose circulatory systems were susceptible and so on.

Later many workers thought that the term hyperventilation syndrome was being used to include too much. Guttman and Jones (1940), Wood (1941), and Friedman (1945) agreed that effort syndrome could not be wholly explained by hyperventilation. The fact remains, however, that the Kerr school has made a valuable contribution in (to quote Gliebe and Auerback (1944) emphasizing hyperventilation "*as an important mechanism of psychosomatic disease – it demonstrates one means whereby emotional disturbances can produce physiological and biochemical changes and physical symptoms*").

World War II focused attention on the occurrence of the hyperventilation syndrome among aircrew. Boothby, while learning to fly, experienced distressing symptoms which he afterward recognized were due to overbreathing and in collaboration with Hinshaw (1941), investigated the effects of hyperventilation on coordination and cerebation. They suggested that the phenomena in pilots of "*blacking out*" and "*freezing to the controls*" might in some cases be due to overbreathing. Hyperventilation at low altitudes was due to emotional stress; at high altitudes, lack of oxygen was an additional factor. Carryer (1943, 1947) was another investigator who emphasized the importance of hyperventilation in aviation medicine.

With the increasing recognition of the syndrome, the various specialties began to contribute knowledge of its manifestations in their own particular fields.

That hyperventilation could produce inversion of T waves in the electrocardiogram was shown as early as 1932 by McGance. This became of increasing importance later because the combination of precordial pain (not uncommon in the hyperventilation syndrome) and electrocardiographic changes led to the erroneous diagnosis of myocardial infarction in anxious patients. In 1943 Thompson demonstrated marked electrocardiographic abnormalities, consisting either of late inversion of T or S-T depression with marked lowering of T in any or all leads of the electrocardiogram during overbreathing in patients with normal hearts. They thought that alkalosis was the main factor in causing these abnormalities.

In 1946 Christensen reported sinus tachycardia, depression of S-T segments, and iso-electric, diphasic, or inverted T waves during overbreathing. He explained them as resulting from interference with coronary blood flow "*by increased intramyocardial tension due to hypocapnia*". In 1947 Scherf

and Schlacluran described lowering of R and T waves in lead 1. They stated that *“as long as a marked increase in heart rate was avoided and the respirations were not sufficiently rapid and shallow to cause anoxia, no depression of the RS-T segment was observed.”* They thought that the changes which did occur resulted from positional changes of the heart.

The co-existence of organic heart disease and hyperventilation was stressed by Stead and Warren (1943) who described patients with compensated heart disease whose *“dyspnoea”* was wrongly attributed to congestive heart failure.

In 1946 Herxheinier reported that asthma could be precipitated in susceptible subjects by overbreathing. He suggested that it might play a part in the pathogenesis of psychologically triggered asthmatic attacks.

In 1947 McKell and Sullivan found that 5.8% of consecutive ambulatory patients with gastrointestinal complaints were, in reality, suffering from the effects of the hyperventilation syndrome. They suggested that anxious patients often got a feeling of fullness which initiated air-swallowing. *“This interferes to some extent with the respiratory rhythm and seems to initiate the hyperventilation in some cases.”*

Engel, Ferris, and Logan (1947) reviewing the subject stated that *“hyperventilation may occur as a more or less nonspecific reaction to the experience of terror, extreme anger, severe pain or other intense emotions in essentially healthy individuals or it may be a symptom of neurosis.”*

They divided the symptoms resulting from overbreathing into two more or less separate groups – one related to the reduction in consciousness and one related to the tetany. They found that there was a close correlation between the *“degree of slowing of frequency of the encephalogram and the degree of reduction of awareness”*. They thought that the symptom of tetany had received an undue amount of attention and that the *“reduction in consciousness develops much earlier and is much more disturbing to the patient”*.

In 1949 Dibden reviewed the subject very fully and stressed the importance of recognizing the syndrome because *“the dramatic demonstration of the nature of the syndrome symptoms by a hyperventilation test so impresses the patient as to create an excellent rapport with the psychiatrist”*.

In 1950 Rice claimed that during 1,000 routine interviews 10% of patients complained of symptoms and signs of the hyperventilation syndrome. He described the symptoms in detail and discussed their pathogenesis.

The present position is, that overbreathing is recognized as a cause of disturbing symptoms; that involuntary overbreathing is a definite clinical entity; that a wide variety of symptoms and signs have been grouped under the term hyperventilation syndrome; and that the most common cause of this syndrome is stress.

## CHAPTER 3 – CLINICAL SYMPTOMS AND SIGNS

This series comprises forty patients who were seen during a two-year period at Groote Schuur Hospital. They were referred for investigation from wards or out-patient departments. Most of them came from the neuro-psychiatric or medical departments. Two came from surgical wards.

Ten cases were hospitalized because of the hyperventilation syndrome (though not diagnosed as such on admission); five cases manifested symptoms and signs of the syndrome while in hospital for other complaints, and twenty-five cases were referred to the out-patient departments with a variety of diagnoses.

### AGE

The oldest patient was 54 years, the youngest 17. The average age was 30.9 years.

- Under 20 years 10 patients
- 20 – 29 years 7 patients
- 30 – 39 years 12 patients
- 40 – 49 years 8 patients
- 50 years and over – 3 patients

### SEX

27 females, 13 males.

### RACE

35 Europeans. 4 Colored. 1 Malay. Clinically almost all systems of the body were involved. Symptoms and signs are described and discussed under each separate system.

## RESPIRATORY SYMPTOMS AND SIGNS

### Symptoms

Twenty-four patients complained of respiratory difficulty, but in only one of them was it the main complaint. Many did not mention it unless asked directly. Only three patients realized that they were overbreathing. The characteristic description of the respiratory difficulty was, *“I could get air into my chest but felt unsatisfied”*, or, *“I felt that I could not get a deep enough breath”*. Associated with this sensation there was often a feeling of being shut in or oppressed. Patients complained that the chest felt *“tight”* and they felt that they must get fresh air. In some cases this led to extraordinary behavior: one man drove through town holding the door of his car open, *“to let in all the air”*; a woman always rushed out of her house, whatever the hour, if she got an attack, *“because I felt I would die for lack of air”*; another patient tore open his collar *“to let all the air in”*.

Two patients complained of *“panting for breath”* during attacks. One complained that she yawned excessively and when a hyperventilation test was done on her she began to yawn uncontrollably after 30 seconds.



Two patients complained that they got a stuffy feeling in the nose at the onset of an attack and were forced to breathe through the mouth. During hyperventilation tests, the majority of the subjects automatically breathed through the mouth.

Previous *“respiratory conditioning”* was seen in three patients; one of them said, *“My wife is asthmatic and watching her struggling for breath makes me feel that I can’t get enough air”*; another woman said, *“my attacks started just after my child died from a gland bursting in her throat and suffocating her”*; a third said, *“I have a congenital heart and doctors are always asking me about my breathing”*.

The respiratory difficulty might come on at any time but occurred most frequently when the subject was tired or upset, in a crowded place, or preparing for sleep. Five subjects were awakened from sleep by respiratory difficulty and occasionally the marriage partner would awaken the heavily breathing subject *“before an attack developed”*.

The characteristic and striking feature of the respiratory difficulty was that it was never related to exertion. If it appeared to be so related, questioning always revealed that it occurred either after or before – never during exertion. Indeed, in some cases, it was actually relieved by some form of physical activity and many patients said, *“When I got the trouble with breathing I was restless and had to walk up and down, and that seemed to help me”*.

The patient in whom the respiratory difficulty was the chief complaint was a man of 45 years, who said that three or four times a week during the previous year he had been getting, attacks when he *“could not get a proper breath”*. This woke him from sleep and he would jump out of bed contorting his body grotesquely in search of respiratory satisfaction. Sweat poured off him, his abdomen became distended and he felt giddy. Attacks lasted about 30 minutes.

Fifteen patients denied any respiratory difficulty.

Interestingly enough seven of these had gross hyperventilation attacks while under observation in hospital. Even at this time, they denied any breathing difficulty. An eighth was instructed to overbreathe and promptly developed one of her *“fits”*. Her mother, who was watching the procedure, said, *“Oh, she always breathes like that during an attack but I did not think it important enough to mention in the history”*.

Two patients said that they did not notice anything wrong with the breathing, *“but my friends always know when I am going to get an attack because my breathing gets so deep.”*

No independent evidence was available of the breathing during attacks of the remaining five patients in this series.

Goldman (1922) claimed that a person must double his respiratory volume before becoming conscious of his breathing. McCance (1932) reports two cases where *“scarcely noticeable overbreathing tetany was induced.”*

## **Signs**

Chronic irregularity of breathing was found in two of ten patients of whom respiratory tracings were taken (Fig. 1 (a) and (b)). Hyperventilation took the form of:

1. Deep, fairly rapid breathing. This was the common type. Subjects usually opened their mouths at this time.
2. Very fast, shallow breathing or panting. This was seen in only two cases. It should be noted that when patients were told to "*pant*" their breathing was still usually deeper than normal.

(Type of breathing after hyperventilation – See Experimental section, page 53).

### **Pathogenesis**

Within a few seconds of overbreathing, the alveolar CO<sub>2</sub> tension drops from the normal of 40 mmHg to 15-20 mmHg. It does not diminish much further despite continued overbreathing. The resulting alkalemia is responsible for many of the clinical manifestations.

## **CEREBRAL SYMPTOMS AND SIGNS**

### **Symptoms**

Thirty-one patients complained of some cerebral disturbance. Twenty-six of them described it as one of several complaints. Where peripheral complaints were prominent, cerebral complaints received cursory mention. The most common complaint was giddiness, faintness, or lightheadedness – never a true vertigo. This sensation was always aggravated by the upright posture and relieved by recumbency. It was often accompanied by blurring of vision or "*black spots before the eyes*". Patients were usually afraid of falling and were unsteady on their feet: one man seldom ventured out of his house because, if he had to cross a busy street, his "*hands and feet would tingle and he would become so giddy that he was afraid he would fall*"; one woman refused to climb stairs because of her lightheadedness. "*A tight band around the head*", or actual headache, was sometimes complained of. Some patients said they felt as if they were drunk and staggered and one woman who had a hyperventilation attack on a bus was actually threatened by the conductor with a charge of drunkenness.

Several patients complained of "*a feeling of unreality*" as though they were not quite in touch with their surroundings. A doctor once described to me a seance which he attended in company with a young girl who had recently been bereaved. He said: "*In the darkness, I could hear her breathing heavily. Suddenly she screamed and as the lights were switched on and a pencil thrust into her hand she scrawled DAD with tetanic fingers. The girl, because of the strange feeling of unreality, was quite sure she had been in touch with the spirit of her dead father*".

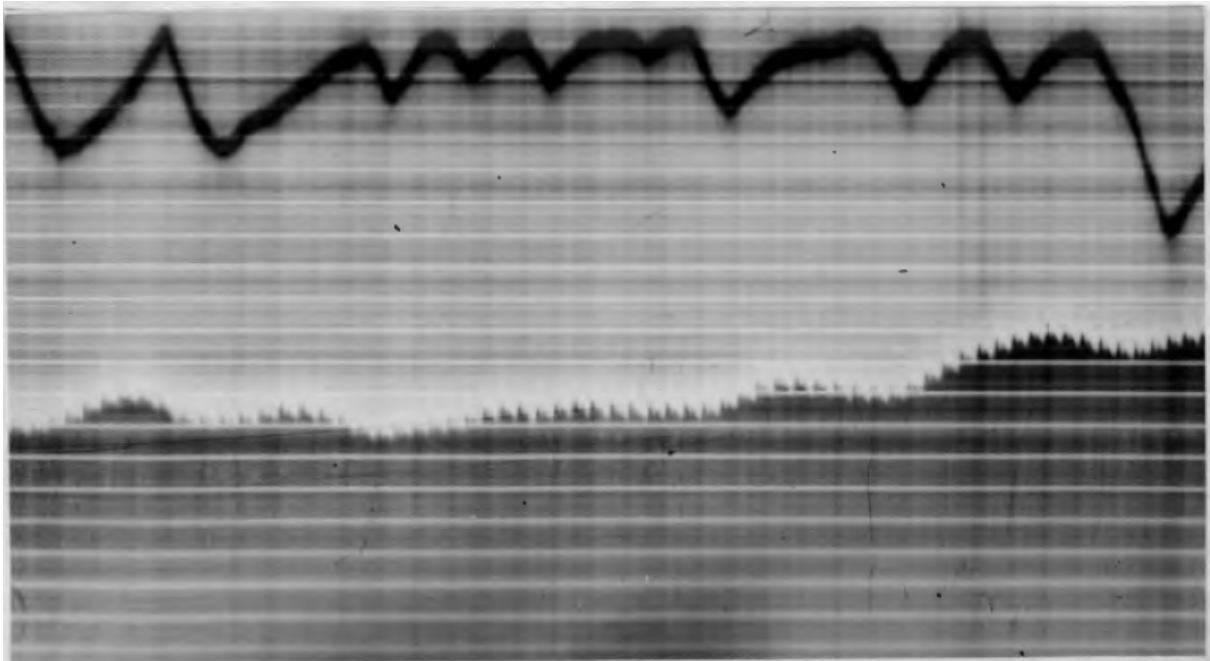


Fig. 1 (a) – Respiratory tracing and plethysmogram of a hyperventilator. This is the “normal” breathing pattern of this patient. Notice the gross irregularity, including involuntary deep breaths. Also, note the small pulse volume.

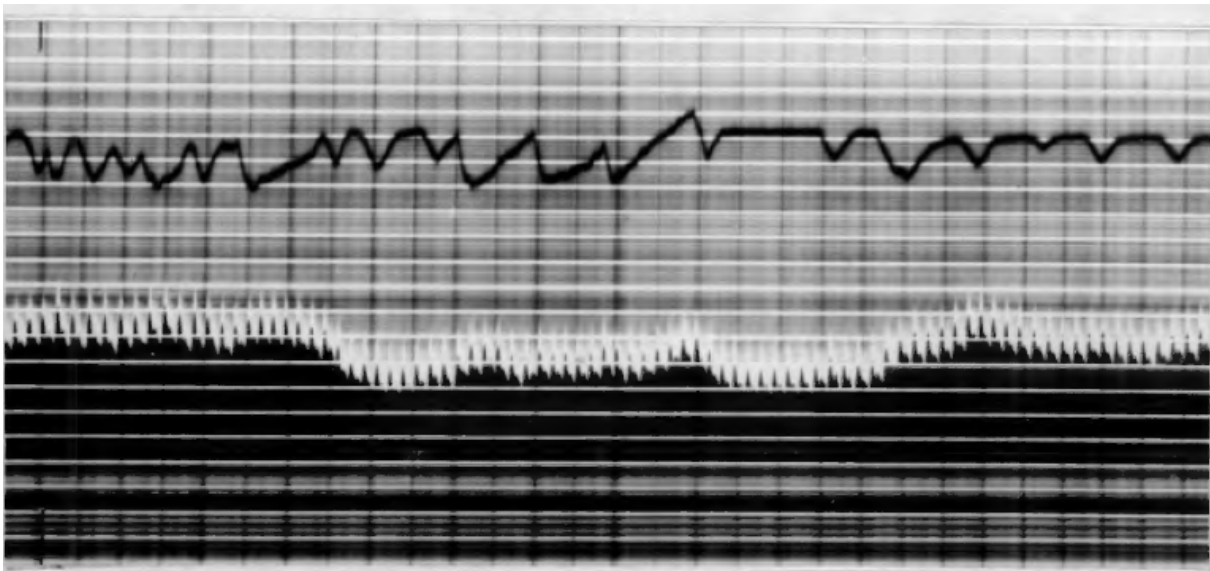


Fig. 1 (b) – Respiratory tracing and plethysmogram of a normal subject when emotionally disturbed. Note that an irregularity of breathing similar to that shown in fig. 1 (a) is present.

Drowsiness – often associated with yawning – was often seen after a hyperventilation test of 2 – 5 minutes. One woman always hyperventilated herself to sleep.

Loss of inhibition is common. Several patients wept or laughed during attacks. For this reason, a hyperventilation test can sometimes be used as a simple abreaction technique.

One patient presented with abnormal behavior as her chief complaint. Her story was that she had been worried for some months about her chest. One morning she had to run to catch a train. She was breathless as she got in and became alarmed at her “*bad chest*”. For the next 20 minutes, she sat on the train with a feeling of “*not being able to get a deep enough breath*”. As the train drew into the station she felt so peculiar that hardly knowing what she was doing, she wrenched open the door of the moving train and fell heavily onto the platform. A hyperventilation test reproduced this “*peculiar feeling*” so exactly that she attempted to get up and run out of the room.

The term “*blackout*” was not infrequently used by patients. This almost always turned out to be a sense of giddiness with a fear of falling but no actual loss of consciousness. Only five patients in this series had a disturbance of consciousness gross enough to merit the term “*blackout*”. (See Appendix-cases 14, 16, 17, 24, 26)

It is interesting that of the nine patients who had no cerebral symptoms always had their hyperventilation attacks when in bed. The recumbent posture diminished cerebral symptoms.

### **Signs**

The disturbance of consciousness can be well illustrated by getting the patient to do a task involving a fair degree of coordination, or to solve an arithmetical problem, immediately after several minutes of overbreathing.

### **Pathogenesis of the Cerebral Symptoms**

The cerebral symptoms point to some definite but easily reversible change in brain activity. This is supported by the fact that there is usually a correlation between disturbance of consciousness and electroencephalographic changes during hyperventilation. Certain of these changes are regarded as indicative of epilepsy.

### **Four types of EEG change may occur**

The most common is the appearance of a high voltage slow rhythm of 2 to 3 cycles per second – the so-called delta rhythm. (See fig.2). The factors which determine the appearance of delta activity are not completely understood. Brazier, Finesinger, and Schwab (1944) working with young adults found that 38% of “*normals*” developed delta activity. All workers agree that delta activity results ultimately from acapnia but they do not agree about the immediate cause. Three possibilities have been suggested – (Hill and Parr, 1950).

- (a) Inadequate compensatory vasoconstriction (Gibbs, Lennox and Nims, 1942).
- (b) Cerebral anemia due to vasoconstriction resulting in anoxia and glucose deprivation (Davis and Wallace, 1942).
- (c) Reduction in the activity of the cholinergic supply to the blood vessels of the cortex resulting in excessive local constriction (Darrov, and Pathman, 1943-44).

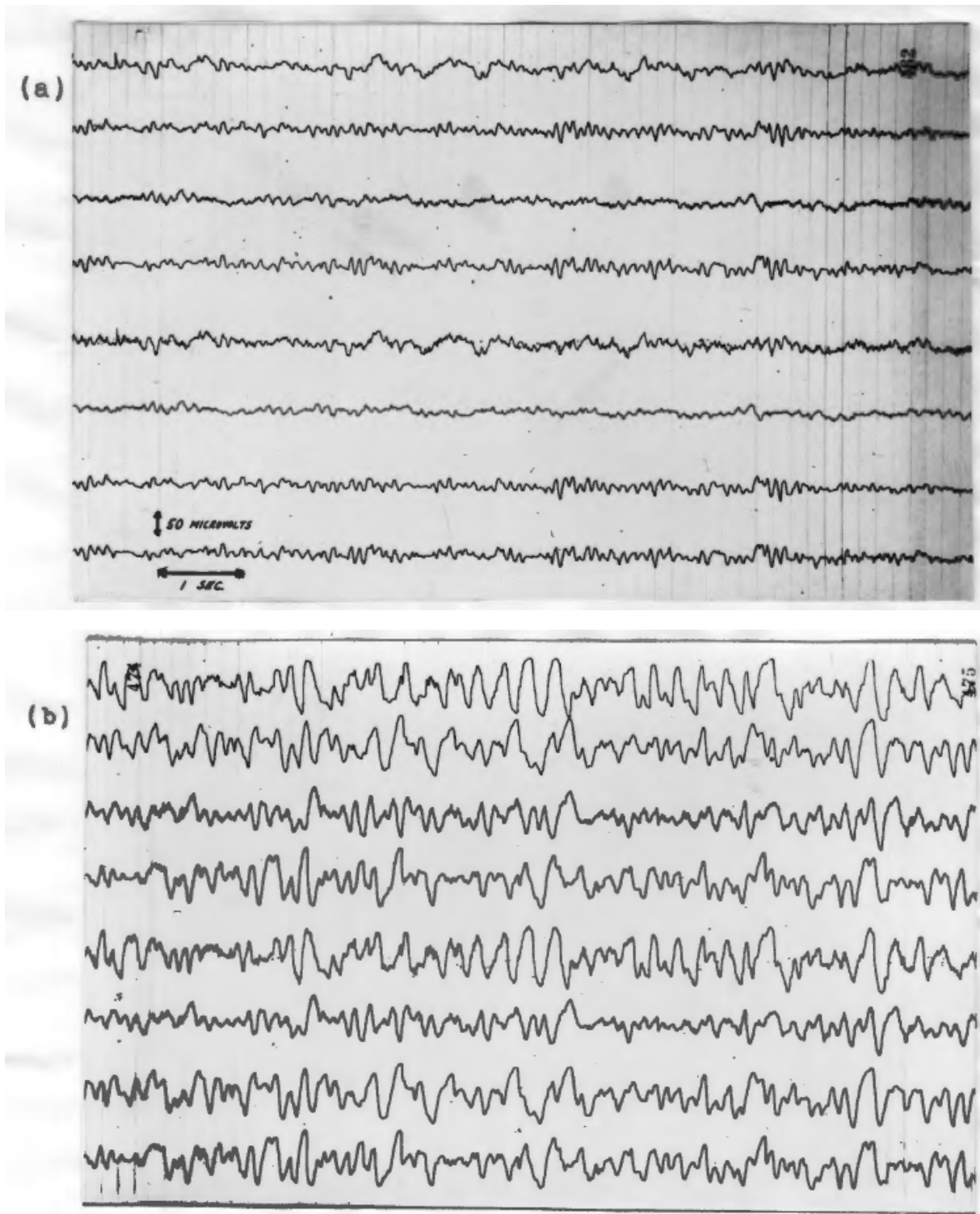


Fig. 2. Electroencephalogram of a subject (a) before 2 minutes of hyperventilation (b) after 2 minutes of hyperventilation. Note the appearance of large delta waves in (b).

It has been suggested that a reasonable working hypothesis is "to regard the delta activity as resulting from a failure of oxidative metabolism in the brain cells and in particular of the oxidation of glucose since the instability may often be prevented by raising the  $O_2$  and glucose levels in the blood". (Hill and Parr, 1950).

It is not unusual, however, for delta activity to appear with no clearly detectable change in consciousness and apparently some subjects can become unconscious during hyperventilation and yet show no delta activity.

The resting alpha rhythm may increase in amplitude without becoming faster than the normal 8-14 cycles per second.

Abnormally fast rhythms may appear or fast rhythms already present may increase in amplitude. If an already existing fast rhythm doubles in voltage or a fast rhythm appears, especially if it appears in bursts, the present tendency is to classify the phenomenon as epileptic.

Both fast and slow rhythms may appear in the well-known spike and wave pattern. This is almost certainly diagnostic of epilepsy. It usually occurs in young patients with petit mal.

These EEG changes disappear within a few seconds when the subject stops overbreathing. It seems that the loss of CO<sub>2</sub> is the fundamental factor. The cerebral circulation is very sensitive to chemical changes in the blood and it is generally accepted that the fall in the CO<sub>2</sub> content of the blood as a result of overbreathing causes the cerebral blood vessels to constrict, thus both reducing the blood flow and conserving CO<sub>2</sub> in the brain. Kety and Schmidt (1946), using the nitrous oxide method, measured changes in cerebral blood flow in five volunteers during active and passive hyperventilation. They found that cerebral blood flow invariably diminished – the mean decrease being 33% during active hyperventilation and 35 percent during passive hyperventilation. The cerebral arteriovenous O<sub>2</sub> difference invariably increased (average 58%) and the cerebral O<sub>2</sub> consumption showed a consistent and significant increase during active hyperventilation (average 15%) but no change during passive hyperventilation.

## **PERIPHERAL NEUROLOGICAL SYMPTOMS AND SIGNS**

Thirty-three patients complained of these.

### **Sensory symptoms**

Sensory symptoms occur earlier than motor. They appear at a variable time after the onset of overbreathing, depending on the rate and depth of breathing and the susceptibility of the subject. Some patients have marked symptoms after two or three deep breaths and others may overbreathe for 5 or more minutes before getting symptoms. The symptoms consist of paresthesia variously described as “tingling”, “pins and needles”, “electric shock”, “deadness” or “numbness”. They always start distally. The usual pattern of spread is first in the fingertips and very often first in the ulnar area; then in the toes and finally in the peri-oral area and tip of the nose. Any one of these sites may be first or solely involved, depending on individual susceptibility. One extremity is frequently involved before the other and it is not necessarily the dominant one; one woman always got her paresthesia in the left hand and around the left side of her face and left ear. She said that her left ear also got deaf during attacks. She was quite sure that this was a form of “stroke”. She was right-handed.

Finally, there may be a generalized tingling. Two patients complained that their teeth were tingling.

A feeling of spasm or tightness in the muscles or the extremities or midline structures, such as the epigastrium or sternum, is a common complaint.

Objective sensory loss then develops in the affected areas. Touch and later pain sensation are interfered with.

### **Motor manifestations**

Motor manifestations consist of fascicular twitching which first involves the face and small muscles of the hands. It may appear spontaneously or be elicited by tapping near a peripheral nerve (Chvostek's sign). Actual tetanic spasm was complained of by six patients – two of whom were alkalotic because of vomiting. If hyperventilation is continued the characteristic spasm of hands and feet develops. On the hand, this consists of adduction and extension of the thumb with extension of the interphalangeal and flexion of the metacarpophalangeal joints. Finally, flexion of the wrist occurs. In the feet the ankles are inverted, tarsus flexed and toes extended. In the face the eyes have a staring look due to contraction of the orbicularis oculi, the jaw is clenched and the corners of the mouth drawn up.

Patients often complain of difficulty in articulation because of “*stiffness*” of the mouth. The larynx may be involved with the production of stridor.

One patient complained of laryngeal stridor, which is uncommon in adults. She was a European female of 52 years who said that four years previously she had had a thyroidectomy. At this operation, her recurrent laryngeal nerve was cut. One month after the operation she was recognized as being myxoedematous. Eight months after the operation she had an attack of stridor. After this, she often woken herself and her family at night by stridor. Her serum calcium is normal. During the day she sometimes got a tingling in her hand and a feeling of “*not being able to get a deep enough breath*”.

Spasm of hands and feet may be painful. It can be relaxed voluntarily, despite continued hyperventilation, if the spasm is not too well established. In one subject who demonstrated this, there was a lag of a few seconds before the hand reverted to its tetanic posture.

Proximal muscles are later involved and if the spread of the spasm is mainly unilateral there may be some diagnostic difficulty: one woman always got tingling in the left hand with drawing up of the left shoulder; the possibility of a Jacksonian attack was considered in her case but the whole picture was reproduced many times by hyperventilation tests.

Muscles of trunk and head area are later involved with the development of opisthotonus. Three cases (not included in this series) were sent to the hospital diagnosed as meningitis because of this marked opisthotonus and neck rigidity. Within a few minutes of cessation of overbreathing, the neck rigidity disappeared and the head assumed its normal position.

The involvement of trunk muscles may be associated with abdominal pain and rigidity. This presented a diagnostic puzzle in two surgical cases. They were both patients with partial intestinal obstruction who had been vomiting and so were in a state of alkalosis. They became alarmed about themselves and began to overbreathe. Tetanic spasm developed and later rigidity of abdominal muscles. The question of perforation then arose but once they had stopped overbreathing the rigidity disappeared.

Marked muscle tenderness may be present in limbs previously the site of tetanic spasm. A nurse was sitting talking to her friends when she developed tingling in her hands and feet. She then collapsed with tetanic spasms in the extremities. After a night of hyperventilation tetany, her muscles were so tender and “*weak*” that she was sent into hospital as a case of poliomyelitis.

Hemi-tetany is very uncommon. Patients often start with paresthesia in one limb but by the time tetanic spasm has been supervened they have generalized symptoms and signs. If, however, there has been some organic nervous disease, especially hemiplegia, hyperventilation may result in hemi-tetany. One such case was a European male of 38 years who one month before hospital admission had developed left-sided hemiplegia due possibly to a vascular accident. His signs cleared up so that clinically there was only minimal evidence of hemiplegia. One morning he woke with his left hand in tetanic spasm. Then he became conscious of a tingling feeling on the left side of his mouth and his left leg became stiff. *"I did not think I was overbreathing but my wife says I was breathing deeply"*. The attack passed off in 15 minutes and he had many such attacks before hospital admission. A hyperventilation test was carried on for 30 minutes. He developed well-marked tetany on the left side with minimal paresthesia on the right. Plethysmography showed no difference in the pulses on the left and right sides.

### **Pathogenesis**

Kugelberg (1946 and 1948) claimed that tetanic activation was ultimately dependent on peripheral nerve change. The pattern of spread was always the same in that the long tactile fibers to the face and hands were first activated, which caused the sensation of tingling. Later other afferents were activated – giving rise to the sensation of spasm. Then the longest motor fibers to the small muscles of the hand were excited (extensors having a lower threshold than flexors). Finally, the shorter fibers to flexor carpi ulnaris were affected.

Kugelberg has done electromyographic studies to show not only the same distinctive type of response but also a distinctive spread of response in all varieties of tetany. He emphasized the primary involvement of the nerves to face and hands and pointed out that these were the parts best represented in the cerebral cortex and most recent phylogenetically. He suggested that the difference in vulnerability of the various nerve fibers might be due to the size of the fiber or to the state of calcium in the fiber.

## **ALIMENTARY SYMPTOMS AND SIGNS**

### **Symptoms**

Many patients complained of dryness of the mouth which was probably due to overbreathing through the mouth.

One patient complained of a bitter taste in the mouth; another of a fishy taste.

Eight patients complained of abdominal distension during an attack. This was usually relieved by belching.

Two patients complained of epigastric discomfort. One of them said, *"During the attack, my stomach feels as though it has turned to jelly"*. Another complained of a *"vice-like"* feeling across the epigastrium.

One patient in this series complained of nausea, and it was complained of by one normal control after a 2-minute overbreathing test.



## Signs

Rigidity of abdominal muscles may be striking during an attack of hyperventilation tetany.

## Pathogenesis

Air swallowing has been suggested as one possible mechanism for the distension. (See fig. 3).

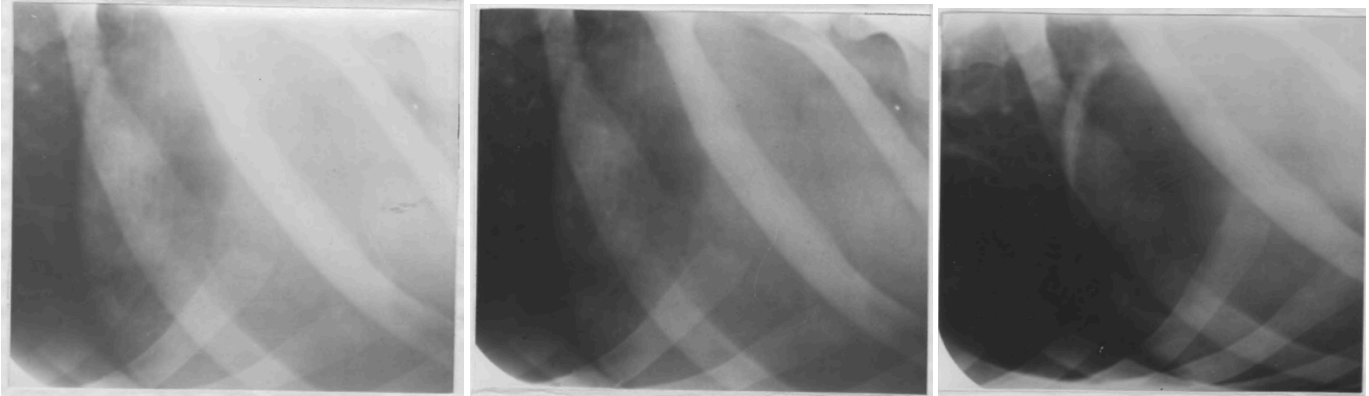


Fig. 3. (a) (b) (c) X-ray of the stomach (a) before, (b) immediately after, and (c) 10 minutes after 5 minutes overbreathing in a normal subject. Note the increase in the amount of intragastric air after overbreathing. The time of exposure and development was constant for all three x-rays.

Another explanation for apparent gross distension is a marked increase in lumbar lordosis. (Westdahl 1951, Roussak 1951). This was seen in a Malay a.man who always became drastically “*distended*” during hyperventilation. Her back was round to be arched several inches off the couch and she refused to relax it saying that it would aggravate her breathing difficulty if she did so.

A tight feeling and rigidity of abdominal muscles are due to increased neuromuscular excitability.

## SYSTEMIC CIRCULATORY SYMPTOMS AND SIGNS

### Symptoms

Eight patients complained of precordial pain. In one case the pain had all the characteristics of angina but was apparently never provoked by any form of exercise other than hyperventilation. One woman got a “*burning*” feeling under the sternum after a few minutes of overbreathing. Another patient complained of “*a sharp pain under the breast bone which shoots up to my left shoulder and around my neck*”. Two patients complained of an oppressive feeling in the left precordium “*as though something is pressing on my heart*.” Another patient complained of a “*dull ache*” over the left precordium. Two patients said they got a sharp stabbing pain “*like a knife*” in the left mammary region.

Ten patients complained of palpitations. In one case it was the sole complaint.

Six patients complained of cold hands and feet, but in only one was it the main complaint. Several patients, after several minutes of overbreathing, complained of a generalized coldness and shivered violently.

Peripheral vasoconstriction was a striking feature in all cases after a few minutes of overbreathing. The hands and feet became cold and sweated freely. Two cases became cyanosed. In some cases, the radial pulse was obliterated. An increase in pulse rate from 6 to 30 beats per minute occurred. In all cases after a few minutes of overbreathing. (See experimental section).

### **Pathogenesis**

Precordial pain of the knife-like or aching left mammary variety might result from the misuse of the respiratory musculature. Any departure from the normal smooth action of breathing might cause fatigue of intercostal muscles or the diaphragm. Wood (1941) invoked diaphragmatic spasm as a cause of the precordial pain seen in Da Costa's syndrome.

The "*pressing pain around the heart*" was relieved in both cases by belching so that distension of the stomach caused by air swallowing might account for this form of discomfort.

Cardiospasm was thought to be responsible for precordial pain in two cases.

Pain that simulates coronary artery disease has led to serious diagnostic errors. Electrocardiographic changes also occur during overbreathing so that the problem may become very difficult. The changes consist of lowering of the S-T segment and lowering or inversion of T waves. There are various theories to account for these changes. Some workers invoke anoxia of heart muscle or coronary vasoconstriction. Others put them down to changes in the position of the heart or associate them with the tachycardia that occurs.

It can be argued that overbreathing is a form of exercise so that true angina could be precipitated by a hyperventilation test. It is also true that some patients with undoubted coronary artery disease hyperventilate through fear and anxiety. Several patients (outside the present series) with definite evidence of coronary occlusion described paresthesia in the limbs as part of the attack. In these cases, careful history taking revealed that the patients had been overbreathing.

Tachycardia is partly explained by the muscular exercise of overbreathing.

The peripheral vasoconstriction that occurs in hyperventilation is dealt with in the experimental section, page 49.

### **Urinary Symptoms and Signs**

Urinary changes which have been reported after overbreathing are alkalinity of the urine, the presence of bicarbonate but little or no ammonia, diuresis, and slight ketonuria.

In this series, two patients complained of diuresis after overbreathing. In six normal controls, the urine became alkaline and showed an increase in phosphates after 8-10 minutes of overbreathing.

### **Pathogenesis**

Some of the urinary changes result from the alkalosis. It is possible that the diminution in cerebral blood flow may partly account for the diuresis or the phosphaturia through a pituitary or hypothalamic mechanism.

The phosphaturia is interesting because, according to Brown and Hilton (1930), it is "*noted most frequently in association with wasting, worry, serious mental depression or severe mental work or strain*".

## **GENERAL SYMPTOMS AND SIGNS**

Fatigue is a common complaint after a hyperventilation test.

### **Pathogenesis**

Hyperventilation is a vigorous form of physical exercise.

## **COMMENT ON CLINICAL EFFECTS OF HYPERVENTILATION**

It is characteristic of the hyperventilation syndrome that, despite its wide and varying pattern of symptoms and signs, the nervous system is always involved. Every case in this series had some evidence of neurogenic dysfunction. Engel, Ferris, and Logan (1947) suggested that patients could be classified according to whether this neurogenic dysfunction was mainly cerebral or mainly peripheral. A grouping of the patients in the present series in this way gives:- mainly cerebral involvement, seven cases; mainly peripheral neurological involvement, nine cases; both cerebral and peripheral, twenty-four cases.

Individual patterns of reaction tend to remain stable in different subjects: a subject whose first symptom is a tingling in the left ulnar region will always tend to start with that symptom.

The pattern is, however, sometimes upset. Among the factors which seem to disturb it are:

- Posture. The upright posture aggravates cerebral symptoms.
- (b) Low blood sugar level. This also aggravates cerebral symptoms. Engel et al. (1947) quoted a case of a woman who always reacted to overbreathing with cerebral symptoms if she was starving and with tetany, if she had just had a high carbohydrate meal.
- (c) Unknown factors. A few subjects vary in their reaction patterns for no apparent reason. A medical man who often acted as a subject in these experiments would on one day manifest tetanic spasm, on another day, cerebral symptoms and yet on other occasions, laryngeal stridor would be an early and striking manifestation.

The time of onset and the severity of symptoms and signs vary both from subject to subject and at different times in the same subject. Some subjects get severe symptoms so quickly after starting to hyperventilate that as a clinical observation they can be classed as hypersensitive. There is at present, however, no satisfactory scientific measure of this hypersensitivity. O'Donovan (1943) defined a hypersensitive person as one who developed tetany within 2 minutes of overbreathing at the rate of 55- 60 breaths per minute, or who was so incapacitated by the severity of the symptoms that hyperventilation could not be carried on for longer than 2 minutes. This does not take into account depth of breathing, or the fact that subjects with a large vital capacity may blow off their CO<sub>2</sub> more rapidly. It also ignores the subjective factor that a person who is tired or feeling demoralized may very quickly feel that his symptoms are too severe to enable him to carry on. Many patients in this series where the breathing rate used were 40 breaths per minute complained that

*“they could not carry on”* when asked to overbreathe for 2 or 3 minutes. Some refused to continue for more than a few seconds. Yet they could not be called hypersensitive to overbreathing in any measurable physiological sense.

Individual sensitivity does not necessarily make one a sufferer from the hyperventilation syndrome, though one is more likely to develop dramatic symptoms if one does overbreathing. Only three subjects, using tetany production within 2 – 3 minutes of overbreathing at the rate of 40 breaths per minute as the criterion for hypersensitivity, could be classed as abnormally sensitive. Two of these were not patients but *“normal controls”*.

Variation in the time of onset and the severity of symptoms in the same subject at different times seemed to be due to fatigue or stress, or both. Patients often remarked that although the symptoms produced in a hyperventilation test were essentially the same as those produced during involuntary overbreathing in response to stress, they were less severe. The physiological and biochemical changes produced in the body during stress lie outside the scope of this thesis. Mention must be made, however, of one factor which may play a part in enhancing the effect or symptoms directly attributable to overbreathing. This factor is that of adrenaline release. Adrenaline is a well-recognized respiratory stimulant; it may be involved in initiating or sustaining the overbreathing. Further, by its action in causing vasoconstriction of skin vessels, adrenaline enhances the reflex peripheral vasoconstriction of overbreathing.

The effect of adrenaline in precipitating tetany in subjects rendered alkalotic by overbreathing has been sporadically investigated for many years. In 1925 Duzar and Hensch claimed that if normal children overbreathed for 5 or 6 minutes they could be made actively tetanic by intravenous adrenaline, without further hyperpnoea. McCance (1932) thought that the only effect of adrenaline administration in aggravating hyperventilation tetany was its action as a respiratory stimulant. Harvey and Lilienthal (1942) found that intraarterial injection of adrenaline in hypocalcemic patients precipitated tetanic spasm. They thought that this was due to the *“abrupt distortion of the potassium-calcium ratio”* which occurs after adrenaline administration and not to the intense vasospasm that also occurred, or to any change in breathing rate. They investigated one subject suffering from the hyperventilation syndrome and reported that adrenaline, without preliminary hyperpnoea, did not precipitate tetanic spasm. But their final comment on this case appears significant: *“after the test, he began moderate, voluntary hyperventilation and induced well-marked carpopedal and facial tetany within one minute”*.

#### **CHAPTER 4 – DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS**

Diagnosis is not difficult if one is aware of the syndrome. It must be made on positive grounds with a clear knowledge of the pathogenesis. If a good history is taken the vast majority of cases give a story of periodic attacks of both peripheral and central nervous system disturbances. Such a story, in the absence of any signs of organic nervous disease, suggests the hyperventilation syndrome. If, in addition, there is respiratory distress unrelated to exertion, the diagnosis is certain. If a case presents with central symptoms alone, or with some other effect or overbreathing, such as tachycardia, the diagnosis may become more difficult. If careful attention is paid to all symptoms, however, and not only to the one which has made the deepest impression on the patient, it is usually possible to elicit the characteristic story of respiratory difficulty associated with paresthesia and giddiness. It must be remembered that patients seldom mention any respiratory difficulty because they are not aware of its relevance. In these cases leading questions are probably justified and the report of relatives may prove helpful.

Finally, a hyperventilation test will clinch the diagnosis. The patient is instructed to overbreathe for several minutes at the rate of 30 or 40 breaths per minute. In this series, most patients reproduced, in 1 to 3 minutes, the symptoms of which they had complained. Some took as long as 8 to 10 minutes. It is important to see that they are really overbreathing and to remember that the upright position is the best one for eliciting cerebral symptoms and the recumbent position the best for eliciting peripheral symptoms. The object of the test is to reproduce the patient's symptoms so that the similarity between the symptoms and those produced by overbreathing is recognized. The time taken to develop the syndrome is not very important, except very broadly, because the depth and rate of breathing vary from patient to patient. A metronome is of help in regulating the rate. Patients also vary from time to time in their susceptibility to the test depending on their emotional state, blood sugar level, etc.

The following are some of the vague or erroneous diagnoses with which these patients presented themselves:

### **Neurosis or "*Functional disease*"**

Fifteen patients were thus diagnosed. In other words, their illness was recognized as being of emotional origin, but no further classification was attempted. There can be no real understanding by the doctor or the patient of an illness vaguely labeled "*neurosis*". If the patient is getting symptoms as real as paresthesia or tetanic spasm his physiology is disturbed. Hyperventilation is one of the mechanisms by which this disordered physical state is brought about.

### **Epilepsy**

Three cases were thought to be epileptic. The diagnosis was made on a story of a sudden loss of consciousness. A careful history showed, however, that all these cases had premonitory signs of respiratory distress. If an attack is witnessed by a doctor the differentiation from an epileptic seizure is easy. In the tetanic "*fit*" the striking thing is the increased rate and depth of breathing. A general stiffening of the body occurs – opisthotonus is marked – but no motor jerking. Occasionally the posture or the hands is unmistakably tetanic. Consciousness is seldom completely lost though the patient may not respond to pin-prick for a few seconds. Tongue biting and incontinence seldom occur. Cyanosis is relatively uncommon though it may occur if overbreathing is followed by a long period of apnea. Many people imagine that grand mal seizures are readily precipitated by overbreathing. Most authorities say it is very uncommon to induce a grand mal seizure in this way though petit mal attacks are readily so induced. Gibbs, Lennox, and Gibbs (1940) claim that patients with petit mal have a low CO<sub>2</sub> level in the blood and so are unusually susceptible to any loss of it through overbreathing.

### **Hypoglycemia**

Three patients were thought to be suffering from hypoglycemic attacks. There are several points of similarity: the periodic nature of the attacks, the excessive sweating, and confusion. However, respiration remains unaffected in hypoglycemia until the patient is deeply comatose and many transient attacks of hypoglycemia are uncommon without some obvious organic disease becoming manifest. One diabetic who was hypoglycemic through insulin overdosage was referred to as a case of the hyperventilation syndrome.

### **Thyrotoxicosis**

The diagnosis of thyrotoxicosis is always difficult and the physical similarity between an anxious and a thyrotoxic patient is well known. Here again, the respiratory difficulty and the reproduction of symptoms and signs by a hyperventilation test are valuable. Two cases in this series were thought to be thyrotoxic.

### **Peripheral vascular disease**

Many doctors who are aware of the hyperventilation syndrome do not realize that one of its manifestations is a striking peripheral vasoconstriction which, because of its periodic nature, may be confused with Raynaud's disease. The relationship to cold is absent, however, and the other manifestations of the hyperventilation syndrome should help to differentiate the two conditions.

### **Poliomyelitis**

One case was admitted to an infectious diseases hospital with this diagnosis because of residual muscle tenderness and a feeling of "*lameness*" in the legs after a night of overbreathing.

### **Organic cardiac disease**

Almost half the patients in this series thought they had heart disease. In some cases, this belief had received support from their doctors. The error on the part of the doctor was usually made because of a lack of careful history taking, a fear of missing something organic, and ignorance of the ECG changes that occur with overbreathing. It is a serious error in an already anxious patient. Two patients had spent 6 weeks in bed – diagnosed as cases of coronary thrombosis. Both these patients described a very severe substernal pain and belching with the attack. They had probably been swallowing air and had developed an associated cardiospasm.

### **Da Costa's syndrome**

Attempts to explain the symptoms of this syndrome by hyperventilation have been made for a long time. White and Hahn (1929) found that 80 of 100 patients with this syndrome had sighing dyspnoea, whereas only 76 of 400 normal controls showed sighing dyspnoea. They concluded that hyperventilation probably accounted for many of the symptoms of Da Costa's syndrome.

Wood (1941) also investigated the problem and concluded that hyperventilation was unimportant in this syndrome. He thought, however, that the left mammary pain common in Da Costa's syndrome might be caused by a habit of breathing intercostally with neglect of the diaphragm and resultant diaphragmatic spasm. There may be an overlap here with the hyperventilation syndrome as left mammary pain is not uncommon.

In 1938 Soley and Shock investigated seven patients in detail and concluded that "*the respiratory alkalosis resulting from hyperventilation produces the symptoms of effort syndrome.*"

In 1945 Friedman said, *“although hyperventilation may occasionally be found in patients with neurocirculatory asthenia, it is not an initial aetiological factor of any real importance in the production of the symptoms from which they suffer”*.

Although there may be some overlap between these two conditions the dyspnoea in De Costa's is characteristically related to exertion, and neurogenic dysfunction which is so striking in the hyperventilation syndrome is absent.

### **Tetany**

Tetanic spasm is not a common feature of the hyperventilation syndrome. It occurred in six patients in this series and two of these patients were alkalotic through vomiting before they hyperventilated. Confusion with other varieties of tetany is unlikely. If difficulty does arise the normal serum calcium level will rule out hypocalcemia and the history will rule out alkalosis from ingestion of alkali or from excessive vomiting.

### **Acroparesthesia**

This condition has in common with the hyperventilation syndrome periodic attacks of paraesthesia in the fingers with no signs of organic nervous disease. Its symptoms, however, are related to posture, not to breathing, and are more often nocturnal. The patient with acroparesthesia often complains of a *“bloated”* feeling or actual swelling of the fingers. Only one hyperventilation patient (outside this series) complained of swelling of the hand during an attack.

## **CHAPTER 5 – TREATMENT**

Much of the treatment is built around the hyperventilation test already described, which is not only diagnostic but for the following reasons, of immense therapeutic importance:

- (a) The majority of patients think that their symptoms are due to some serious organic disease. The reproduction of these symptoms by overbreathing does more than any words can do to assure them that either no serious organic disease is present, or, if such disease is present, it is not the cause of the symptoms and should be dealt with as a separate problem. A not uncommon example of the co-existence of the syndrome with organic disease is the patient who has had a cardiac infarction and has become anxious about his heart. The anxiety results in hyperventilation which causes distressing symptoms. The patient automatically assumes that these symptoms indicate that his heart condition is worse.
- (b) During the test the patient is shown how much more difficult it is to hyperventilate through the nose and the value of nasal breathing in preventing hyperventilation is emphasized. Air swallowing is impossible with nasal breathing.
- (c) Some observers, impressed by the predominantly intercostal character of these patients' breathing, stress the importance of teaching them to breathe abdominally.
- (d) A demonstration of the relief gained from symptoms by breath-holding or by re-breathing into a paper bag or hat etc., is an essential part of the test. Breath-holding is ideal because it not only relieves the symptoms which result from loss of CO<sub>2</sub> but also relieves symptoms such as peripheral vasoconstriction, tachycardia, etc., which result from the mechanical act

of overbreathing. Many patients, however, find it impossible to hold their breath because the sensation of “*not getting enough air into the chest*” is so overpowering. If they re-breathe into a bag or that the relief of the alkalotic symptoms usually eventually stops the hyperventilation

Medication is usually not necessary apart from sedation in anxious patients. For this purpose phenobarbitone, ½ – 1 grain three times a day, and sodium amytal 1 – 3 grains at night is useful.

Calcium is of doubtful value. Many patients have been given calcium gluconate intravenously by their doctors during attacks or hyperventilation tetany and said that it relieved their symptoms. It is possible that the mere fact of calling in a doctor was so reassuring that they stopped overbreathing. It is not justifiable to keep a patient on regular calcium or vitamin D medication. O’Donovan’s claim that such therapy abolishes hypersensitivity to the effects of overbreathing is an isolated report and the therapy is not without danger.

Kerr, Oliebe, Soley, and Shock (1939) found ammonium chloride of value in “*acidifying*” their patients so that it became more difficult for them to become alkalotic if they did overbreathe.

The emotional stress which has caused the hyperventilation usually needs to be treated. The association between breathing disorder and stress is explained to the patient and he is given the opportunity to discuss his emotional problems. Occasionally this happens quite spontaneously immediately after a hyperventilation test because of loss of cortical inhibition.

No attempt was made to do any extensive psychoanalysis on the patients in this series. Patients appeared to adjust themselves well if given an early opportunity to discuss their problems.

Psychotherapy is not always necessary. Some patients, once shown the technique for breaking the vicious circle of symptoms from which they are suffering, appear able to make a good general adjustment on their own.

The technique of progressive relaxation was taught to all patients who were very tense.

## **CHAPTER 6 – EXPERIMENTAL INVESTIGATION OF THE PERIPHERAL VASCULAR PHENOMENA OF THE HYPERVENTILATION SYNDROME**

### **HISTORICAL REVIEW**

It is more than 50 years since the association between deep breathing and peripheral vasoconstriction was first noted. Binet and Sollier (1895) were the first authors to mention that a diminution in finger volume occurred with deep breathing. In 1924 Uhlenbruck again mentioned this association.

In 1933 Goetz demonstrated that a single deep breath produced a profound peripheral constriction. Associated with this he recorded a decrease in skin temperature, a drop in the rate of blood flow, and a slowing, and, in some cases, a stasis in capillary blood flow.

In 1935 Goetz made a detailed study of the effects of a single deep breath and concluded that the diminution in blood flow was reflex since it was abolished by sympathectomy. Peters (1939) thought that the afferent stimulus came from the lungs themselves.



In 1936 the first comprehensive description in English was written by Bolton, Carmichael, and Sturup. They, like Goetz, thought that the diminution in finger volume was due to a reflex whose efferent path was the sympathetic and whose afferent stimulus probably resulted from the expansion of the chest wall. They did not obtain vasoconstriction with purely abdominal breathing.

In 1939 Mulinos and Shulman, using several different methods showed that a deep inspiration caused marked vasoconstriction of the arterioles of the forearm and hand. They observed a complete standstill of blood in the capillary tufts, persisting for 3 to 5 seconds, after a deep breath.

In 1948 Gilliat showed that the fall in systolic pressure which accompanies a deep breath was not responsible for the peripheral vasoconstriction. He then described the reflex vasoconstriction in detail – saying that a single deep breath caused a diminution in finger volume of the order of 0.5 – 1% while the volume of each pulse decreased to 50% or less of its former value. The latency of the response was about 3 seconds and the finger usually regained its previous volume in 60 seconds. The constriction also occurred with passive inflation of the chest and did not occur after obstructed inspiratory or expiratory efforts. He disagreed with Bolton et al. about the lack of response with abdominal breathing and claimed that vasoconstriction did occur with fast rates of abdominal breathing.

In a separate article in 1948, Gilliat attempted to define the exact afferent pathway of the reflex. After experimenting with paraplegics he concluded that the afferent pathway entered the spinal cord mainly in the upper thoracic region but the possibility that the *“limits of entry are somewhat wider was not excluded”*.

The reflex peripheral vasoconstriction after a deep breath has been invoked to explain the peripheral vasoconstriction after a deep inhalation of an unlighted cigarette (Goetz, 1942) and has been used to test for any regeneration of sympathetic fibers after a sympathectomy.

## **METHODS AND MATERIAL**

The state of the peripheral circulation under various conditions of breathing was studied.

Digital and pulse volumes were recorded by means of the optical digital plethysmograph described in detail by Goetz (1948). Briefly, the method consists of enclosing the finger or toe in a plethysmograph which is made airtight by sealing it with vaseline. The plethysmograph is connected to a specially made pipette graduated in 100ths of a ml. A column of alcohol is run into the pipette and any change in digital and pulse volume is transmitted to this column. The movements or the meniscus of the column are projected onto the paper of a recording camera. The .01 ml graduations of the pipette appear as white lines in the plethysmogram and serve as calibration for volume changes.

A 2-second time marker facilitates the calculation of the pulse rate. The respiratory tracing is recorded simultaneously by placing a cylinder of corrugated rubber around the subject's chest. This is connected by tubing to an all-metal pressure capsule, designed by Goetz, and any movement of the chest wall is reflected on the plethysmogram.

With this apparatus, the following can be read from the plethysmogram:

- The pulse volume and shape of the pulse wave
- The digital volume
- The pulse rate
- The depth, rate, and regularity of respiration

The venous congestion test was done on a finger using the method recommended by Goetz (1943). Briefly, the method consists of the sudden inflation to 50 – 60 mmHg of a cuff placed around the forearm. This amount of inflation is sufficient to impede the venous return without interfering with the arterial inflow. The venous bed of the finger is normally only partly filled and during the first few seconds of the test is able to take up the arterial input without resistance. Consequently, the rate of increase in volume during this period is, graphically, practically a straight line and the rate of blood flow can be calculated from it.

The gas flow was from a cylinder to a reservoir bag, connected to a B.M.R. mouthpiece via a nonreturn expiratory valve mounted at the mouthpiece. A B.M.R. nose clip was used. Warming and moistening the gas was done by introducing a Woulff's bottle containing warm water into the circuit.

Eight members of the series were used. Many of the normal controls were colleagues. All these subjects were free of organic vascular disease and stable enough to cooperate in the experiments. Some subjects were used several times.

Three patients who had had operations for removal of sympathetic ganglia were used. One of these had had a complete sympathectomy for hypertension. The other two were young women with acrocyanosis who were treated at varying intervals after a two-stage sympathectomy of the upper limbs.

All subjects reclined on a specially made couch with limbs nearly horizontal. They were instructed to relax in this position in a quiet dim room for 30 minutes before experiments were begun. The posture of the patient is important as marked changes in pulse volume result from a change in posture (Goetz and Ames, 1949. Goetz, 1950).

### **The normal plethysmogram**

While the experimental part of this thesis is concerned with the peripheral vasoconstriction caused by deep breathing, certain other facts relating to changes in the peripheral vascular system are mentioned here because they may be important in the interpretation of some of the results obtained.

In the normal subject, even at rest, digital and pulse volume may show waxing and waning which coincides with the respiratory cycle. These changes are usually explained as a result of the proximity of the vasomotor and respiratory centers in the medulla. (Fig. 4.) The changes can be induced or accentuated in a normal subject by adding CO<sub>2</sub> to the mixture breathed (Fig. 10 ( b)).

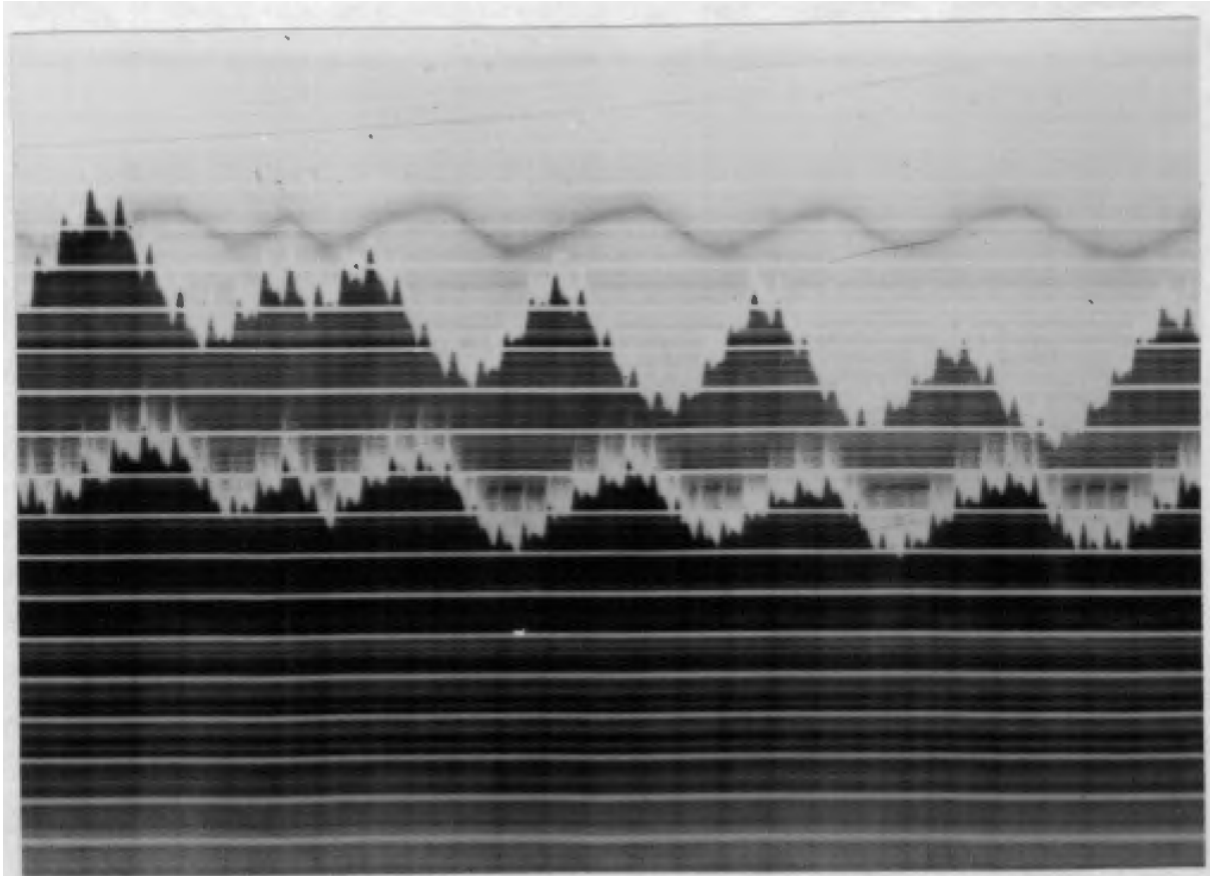


Fig. 4. *Plethysmogram of left index finger (upper tracing) and left big toe (lower tracing). The subject at rest. Note fluctuations in digital and pulse volume with respiration.*

Goetz (1937) suggested that this did not result from the increased depth of respiration with CO<sub>2</sub> but that the CO<sub>2</sub> itself acted as a vasomotor stimulant.

In addition, there are certain well-known extrinsic stimuli causing peripheral vasoconstriction. These are mental activity; any sensory stimulus, e.g. pain; noise; a yawn; a sigh. Mental activity and a sensory stimulus produce a similar plethysmographic response. The peripheral vasoconstriction caused by them comes about independently of respiration. The degree and duration of the vasoconstriction are similar to that caused by a single deep breath ( Fig. 5 and 6). A yawn and a sigh are in effect variants of a deep breath.

## INVESTIGATIONS

Three aspects of the peripheral vasoconstriction associated with breathing were investigated.

1. The effect of variations in a single breath.
2. The effect of 2 minutes of overbreathing.
3. The effect of overbreathing:
  - a. in ten subjects with one hand cooled and the other warmed.
  - b. in ten subjects with elevated limbs.
  - c. in two subjects with acrocyanosis. at varying intervals, after the upper limbs had been sympathectomized.
  - d. in a subject with total sympathectomy.

## 1. The effect of variations in a single breath

(a) The usual response to a single deep breath is a considerable reduction in pulse volume. This occurs about 3 seconds after inspiration has begun and appears to coincide with the climax of the inspiratory phase. It is maximal from the beginning and a return to the original pulse volume takes about 30 seconds. (Fig. 7).

The vasomotor tone is normally higher in the legs than in the arms if the subject is standing or reclining. As the subjects were reclining during these experiments toes were recorded less frequently than fingers because their low initial pulse volume made some of the results difficult to interpret.

The fact that toes do also constrict rules out the possibility that the vasoconstriction is due to compression of arm arteries by the movement of the shoulder girdle that accompanies a deep breath. (Fig. 8)

Coinciding with the diminution in pulse volume there is a corresponding reduction in arterial inflow, (Fig. 9 (a), (b), and (c)).

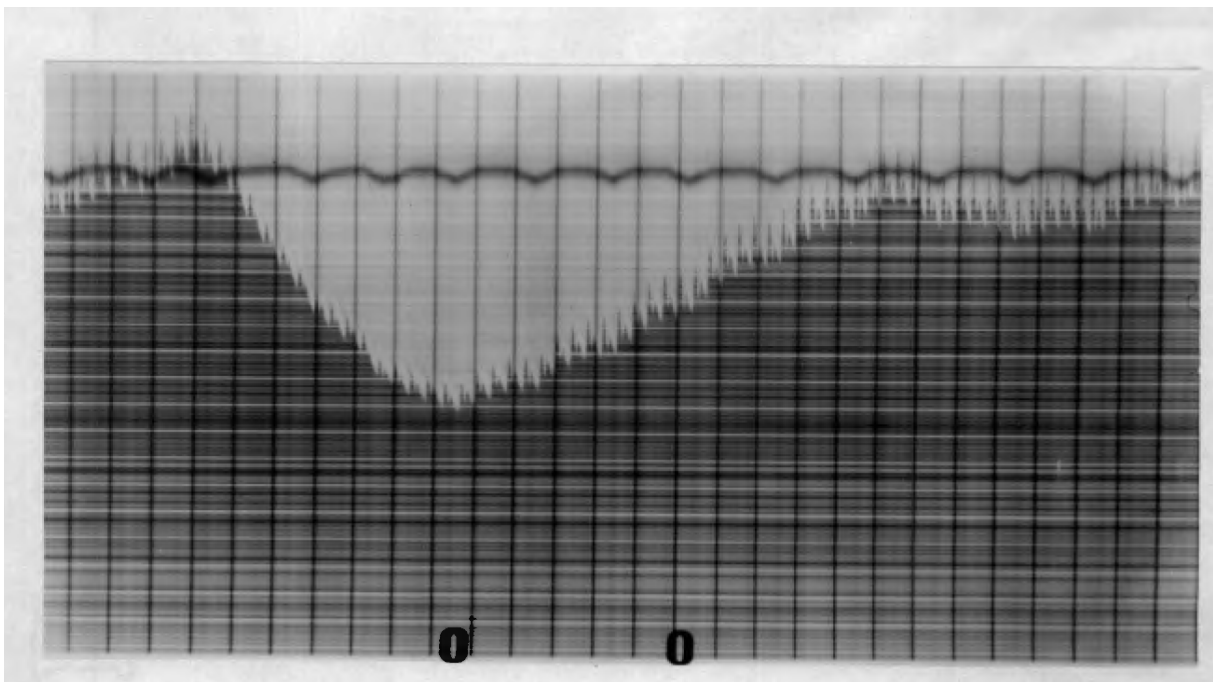


Fig. 5. Plethysmogram of the left index finger. Subject doing mental arithmetic. The period of calculation is indicated by the numbers. Note the vasoconstriction which begins while the subject is being given the calculation.

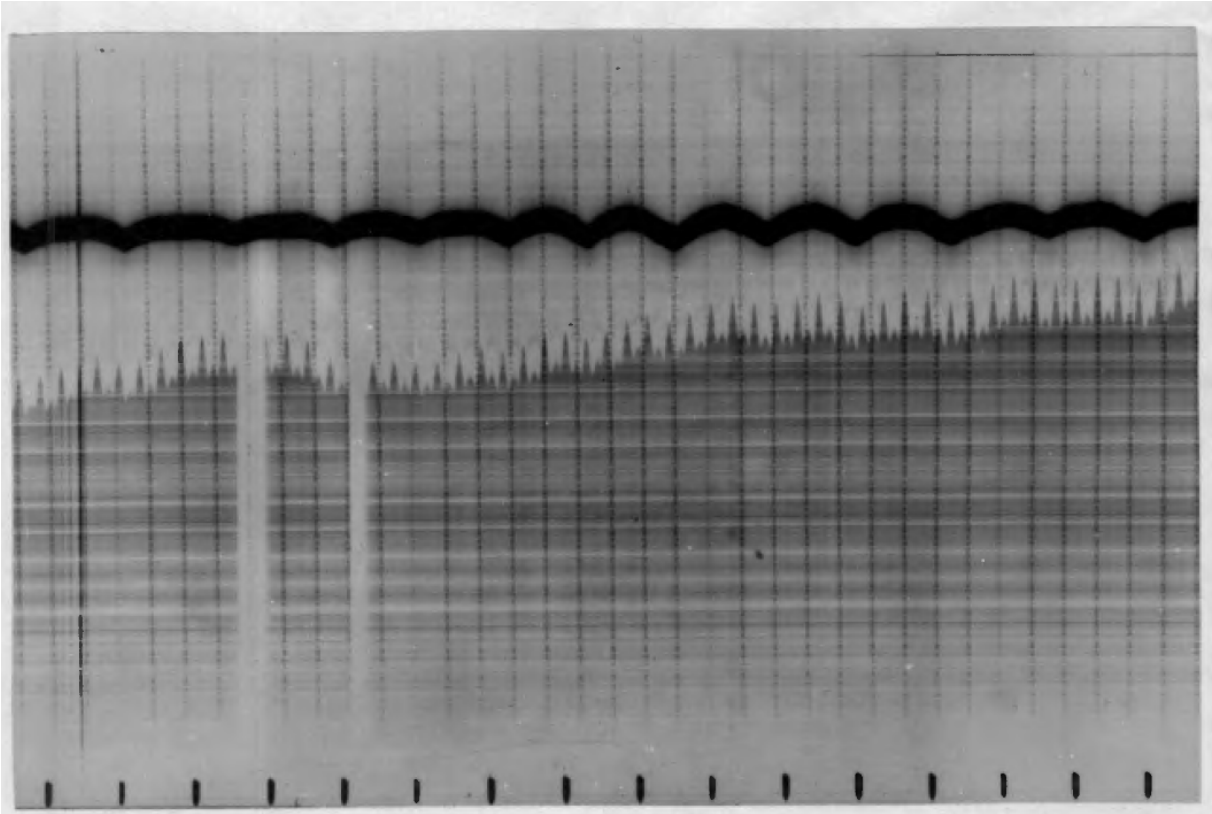


Fig. 6. Plethysmogram of the left index finger. A sudden noise was made by dropping a basin. Duration of the noise indicated by vertical white lines. Note the vasoconstriction.

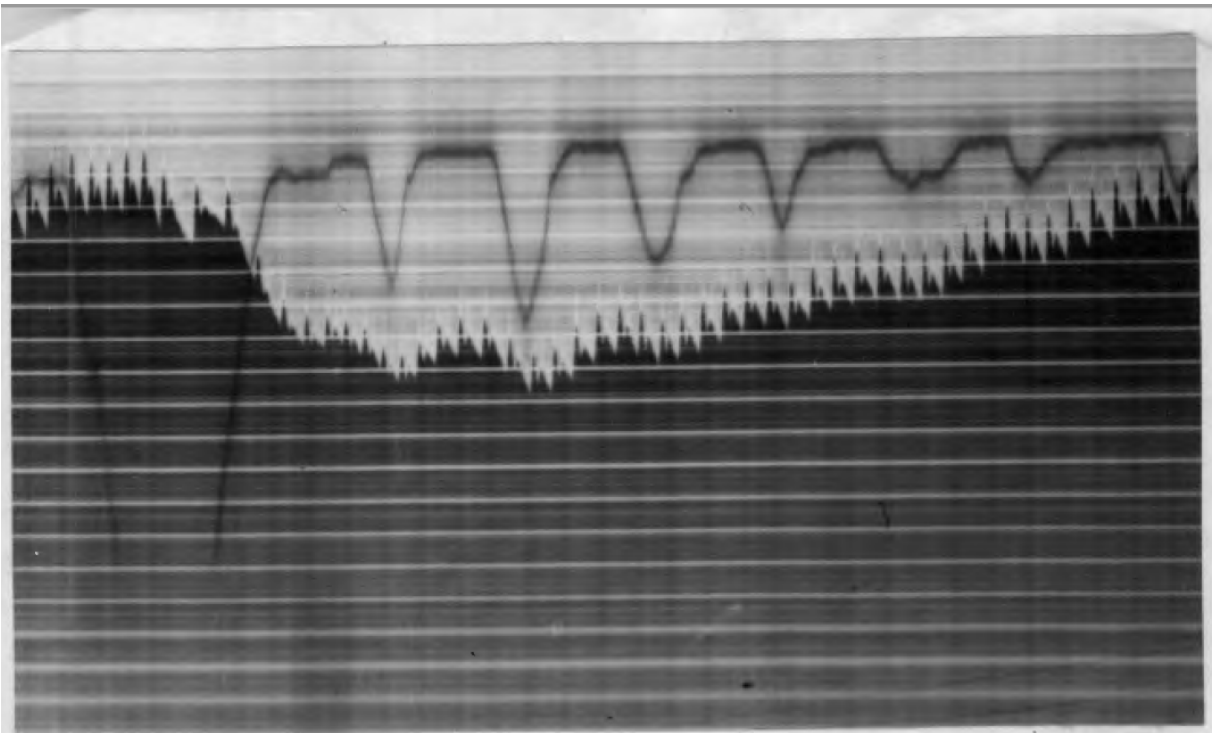


Fig. 7. – Plethysmogram of the left index finger. Subject instructed to take one deep breath. Note vasoconstriction which takes a few seconds to occur and is considerable.

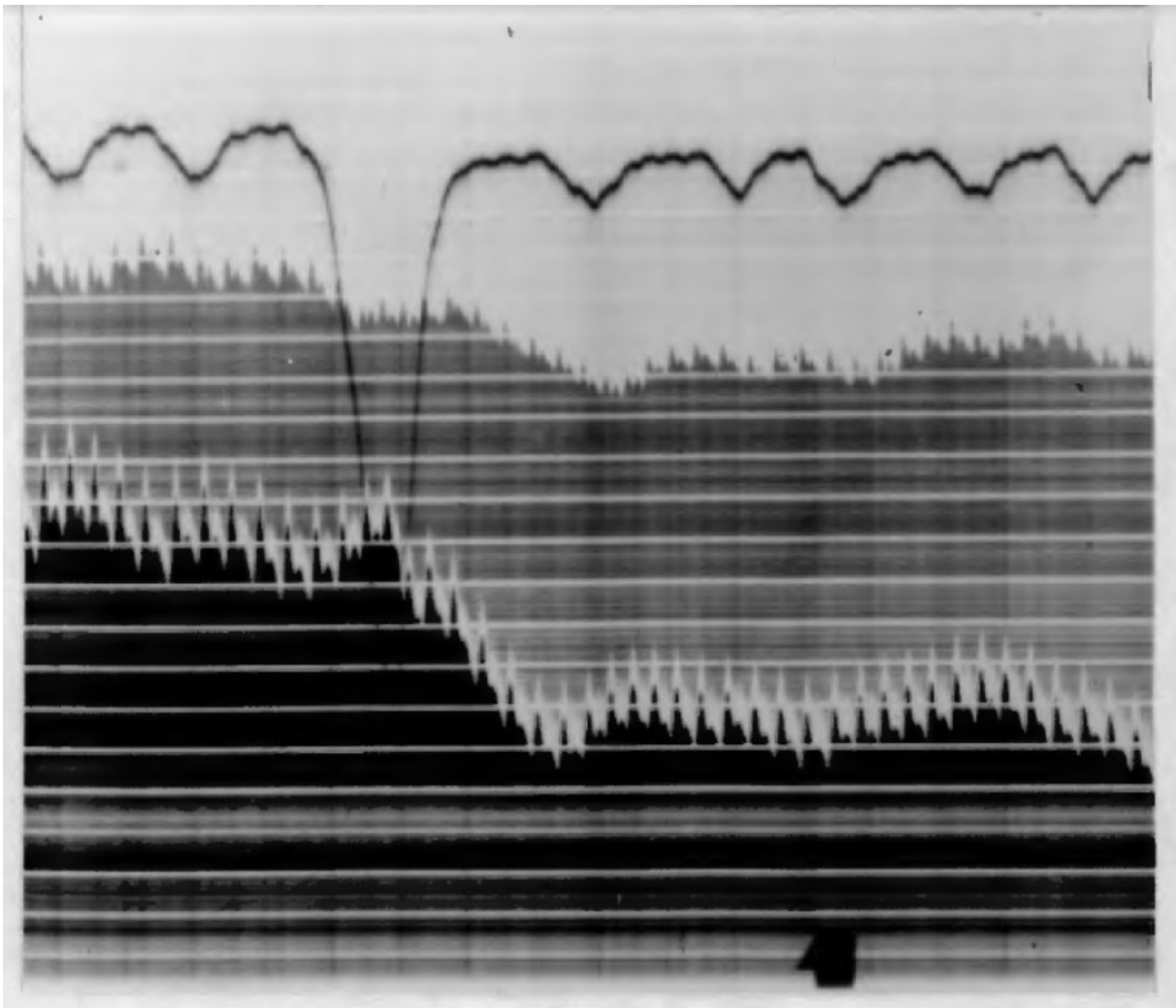


Fig. 8. – Plethysmogram of the left index finger (lower tracing) and left big toe (upper tracing). Subject instructed to take one deep breath. Note vasoconstriction in the toe as well as the finger.

(b) This characteristic peripheral vasoconstriction after a deep breath occurred whether air, oxygen, or a mixture of air and 4 1/2 percent CO<sub>2</sub> was breathed. (Fig. 10 (a), (b) and (c)).

It also occurred if the inspired gas was warm and moist or cold and dry. This latter point is of some importance as a cold stimulus to the sensitive nasal mucous membrane sometimes produces reflex vasoconstriction.

(c) The depth of breath is important. Vasoconstriction did not occur with a deeper than normal but still fairly small breath. (Fig. 11 (a) and (b)). It did occur, however, with rapid, shallow breathing. (Fig. 12).

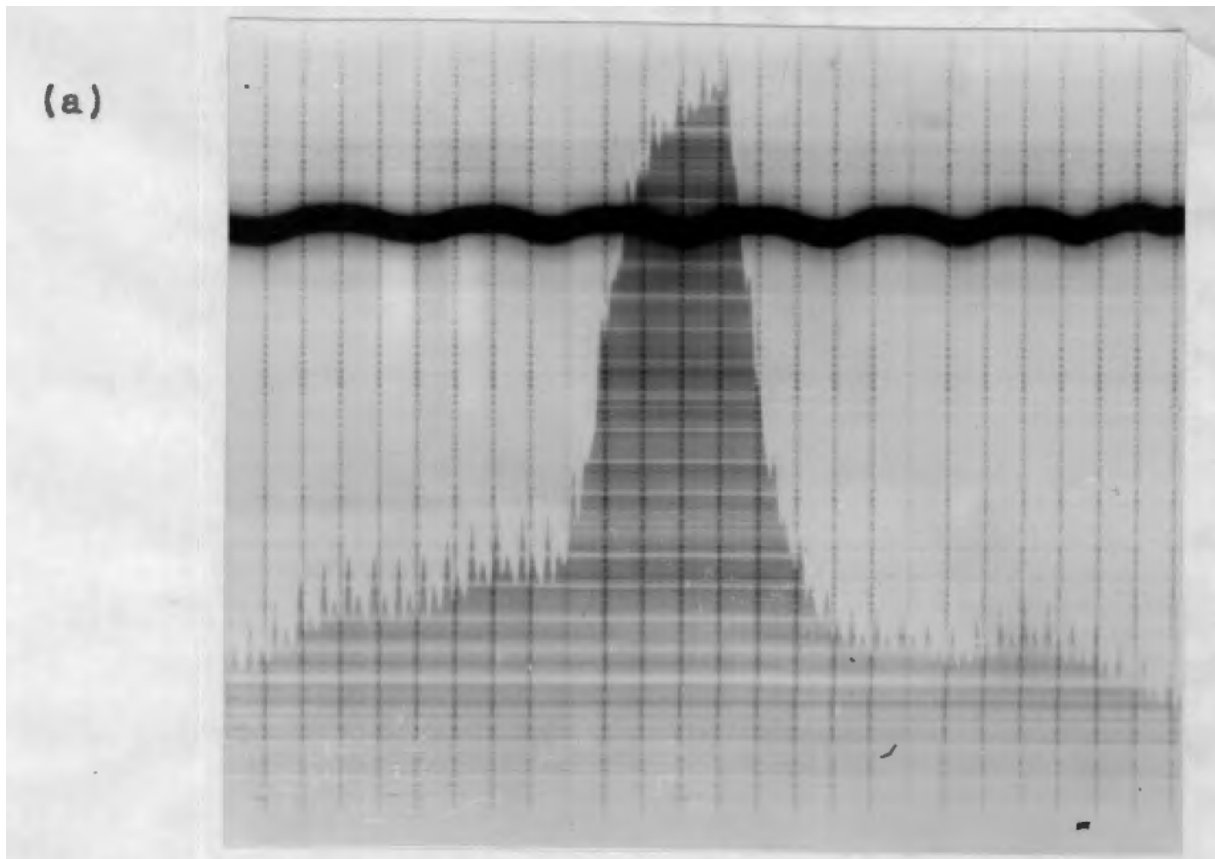
(d) Vasoconstriction did occur with an attempt to take a deep breath against a closed glottis. (Fig.13).

(e) Vasoconstriction did not occur with a purely abdominal breath. This is not surprising because the breath taken in this way was always a small one.

(f) Vasoconstriction did not occur in limbs to which the sympathetic supply had been removed. This supports the commonly accepted view that the afferent path for the vasoconstrictor reflex is sympathetic. (Fig. 14 (a) and (b)).

(g) The response to a single deep breath was compared in eight normals and eight hyperventilators. Subjects were matched for age and sex as far as possible. (Table I).

A summary of the results shows that in normals, the average initial pulse volume was 0.0151 ml, a single deep breath reduced this to 0.0073 ml., and this vasoconstriction persisted for an average of 30 seconds. In hyperventilators the average initial pulse volume was 0.0083 ml, a single deep breath reduced it to 0.0037 ml, and this vasoconstriction persisted for an average of 24 seconds.



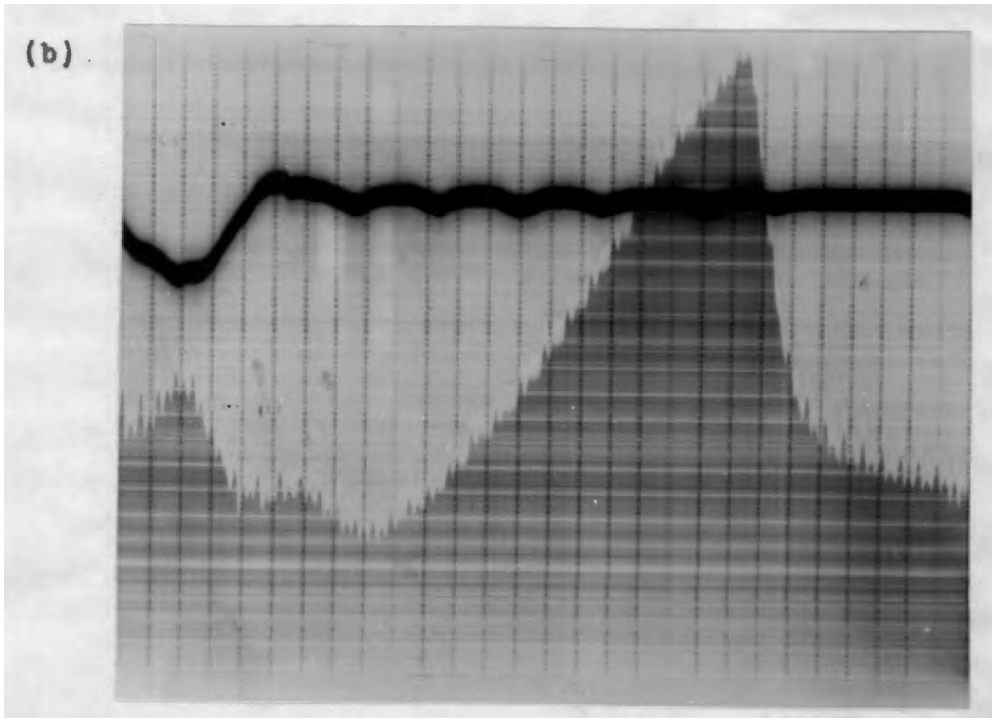


Fig. 9. (a) and (b) Plethysmogram of right index finger during venous congestion tests. Note that in (a) the pulse tracing shifts upwards at almost 90 degrees, reflecting a rapid increase in digital volume and consequently a rapid arterial inflow. In (b) the tracing moves upwards at an angle of about 45 degrees, showing the slower arterial inflow following the vasoconstriction after one deep breath.

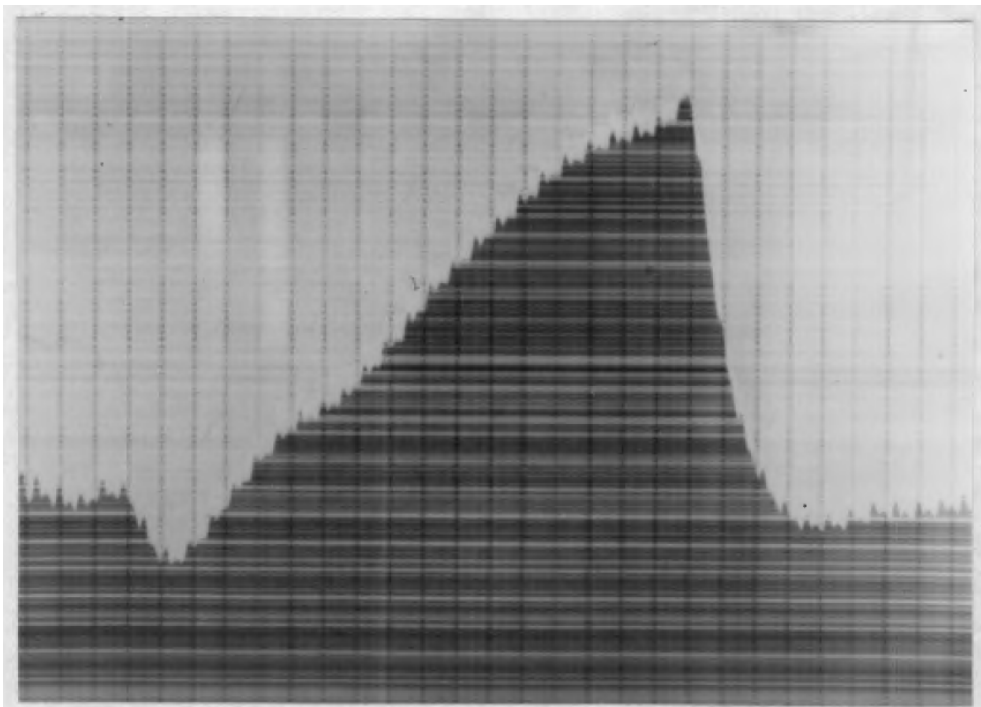


Fig. 9. (c) Plethysmogram of right index finger during venous congestion test after two minutes hyperventilation. Fig. 10 (a) Plethysmogram of the left index finger. Subject breathing air. One deep breath was taken. The apnoea is voluntary. Note vasoconstriction.



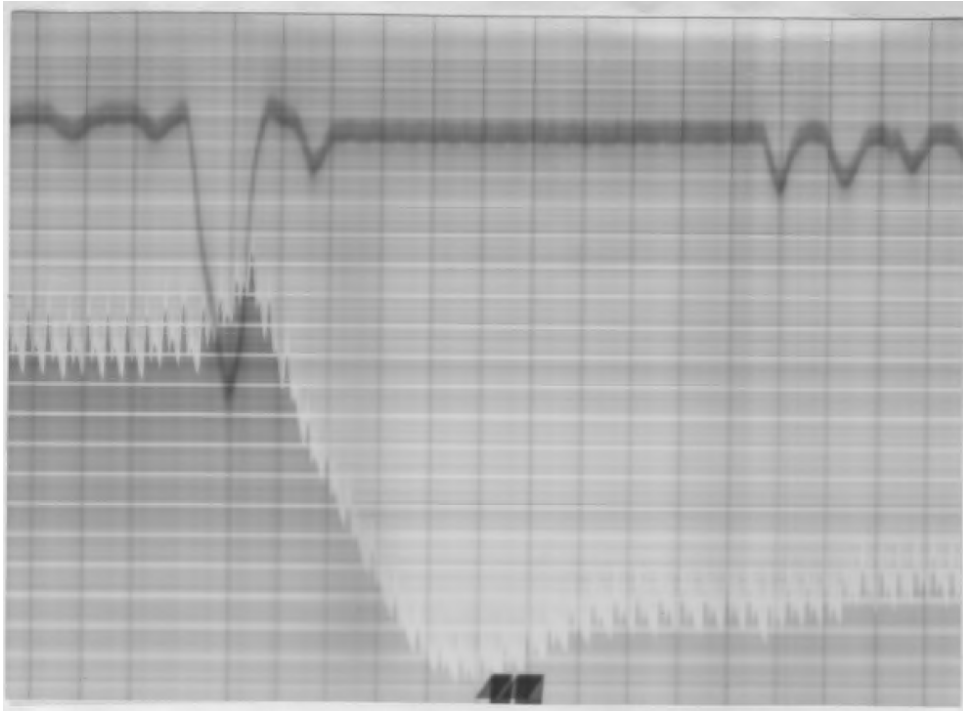


Fig. 10 (a) – Plethysmogram of the left index finger. Subjects breathing air. One dee breath was taken. The apnoea is voluntary. Note vasoconstriction.

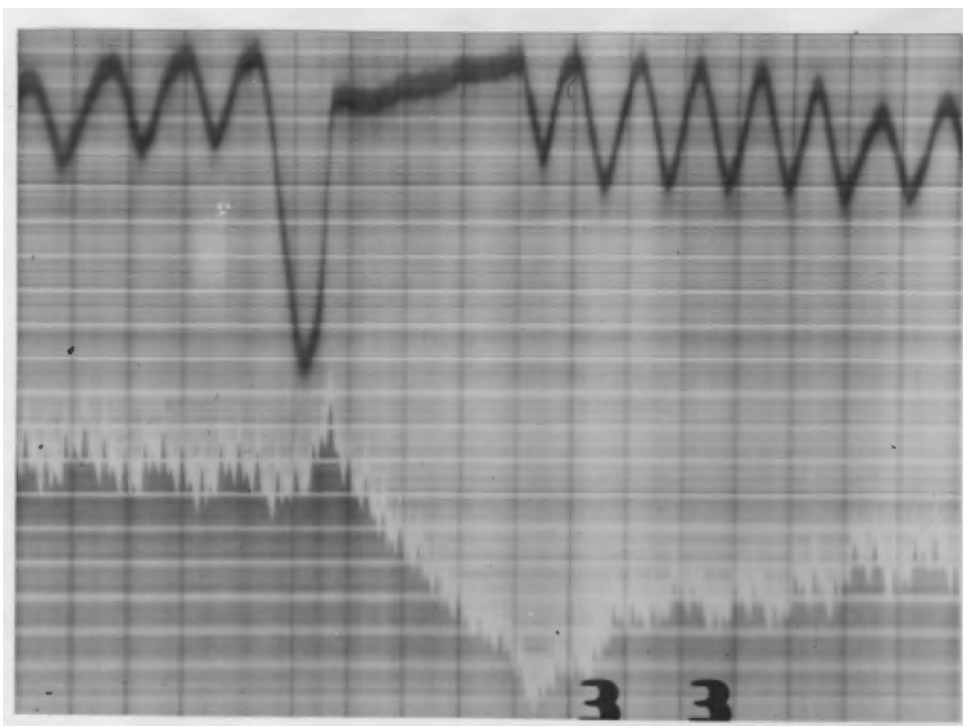


Fig. 10 (b) – Plethysmogram of the left index finger. Subject breathing a mixture of air and CO<sub>2</sub> (4 percent). One deep breath is taken. The apnoea is voluntary. Note vasoconstriction. Also, note the appearance of spontaneous fluctuations in digital and pulse volume. The same subject was used for fig 10 (a) and fig. 10 (b). Both tracings were recorded during the same experiment.

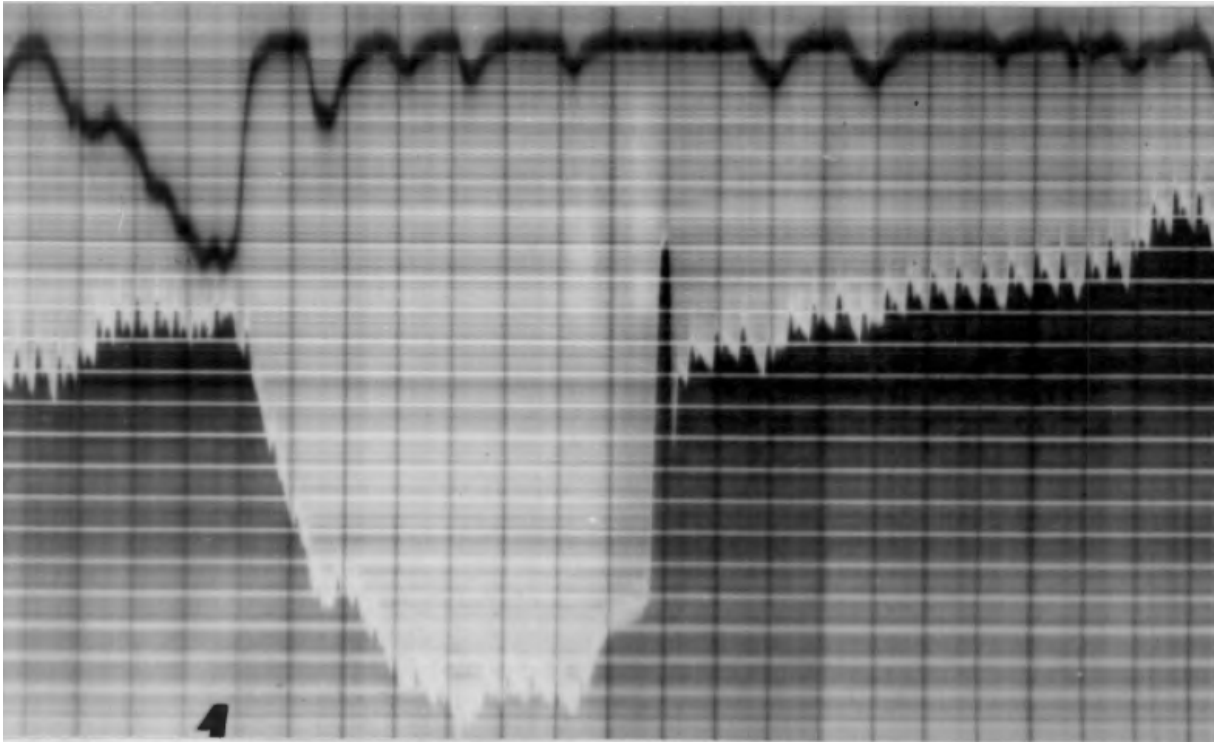


Fig. 10 (c) – Plethysmogram of the left index finger. Subject breathing oxygen. One deep breath was taken. Note the vasoconstriction.

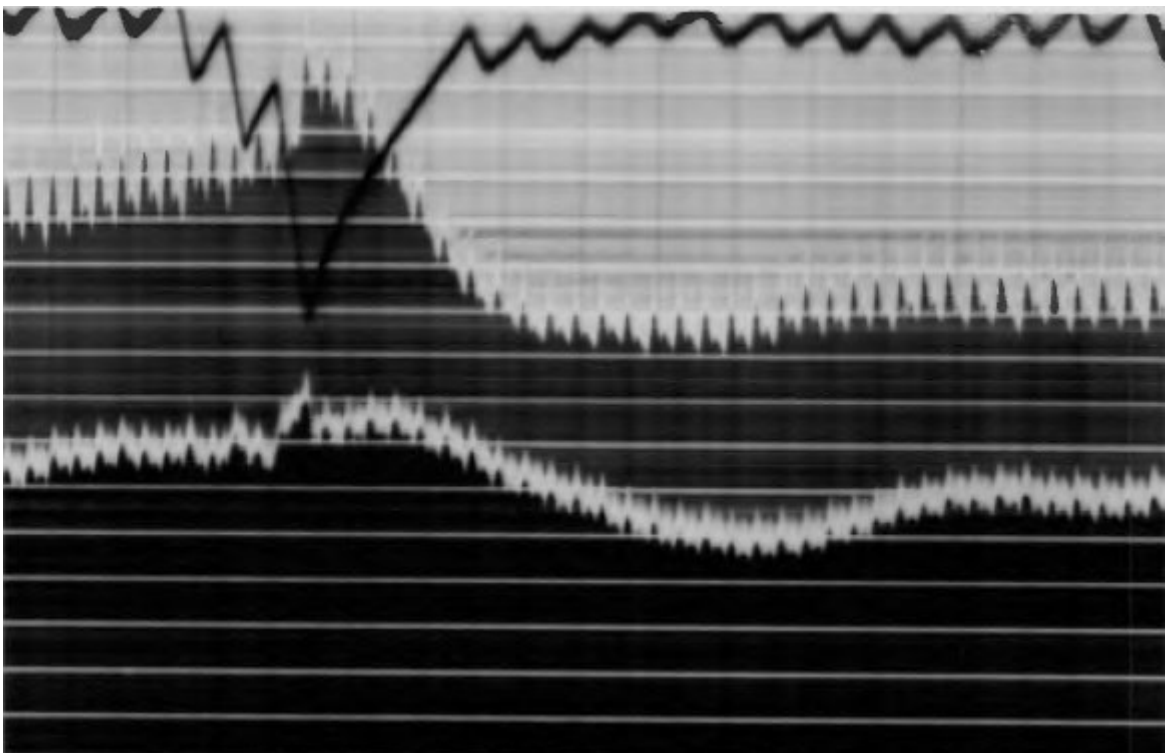


Fig. 11 (a) – Plethysmogram of the left index finger (upper tracing) and left big toe (lower tracing). One deep breath was taken. Note the vasoconstriction.

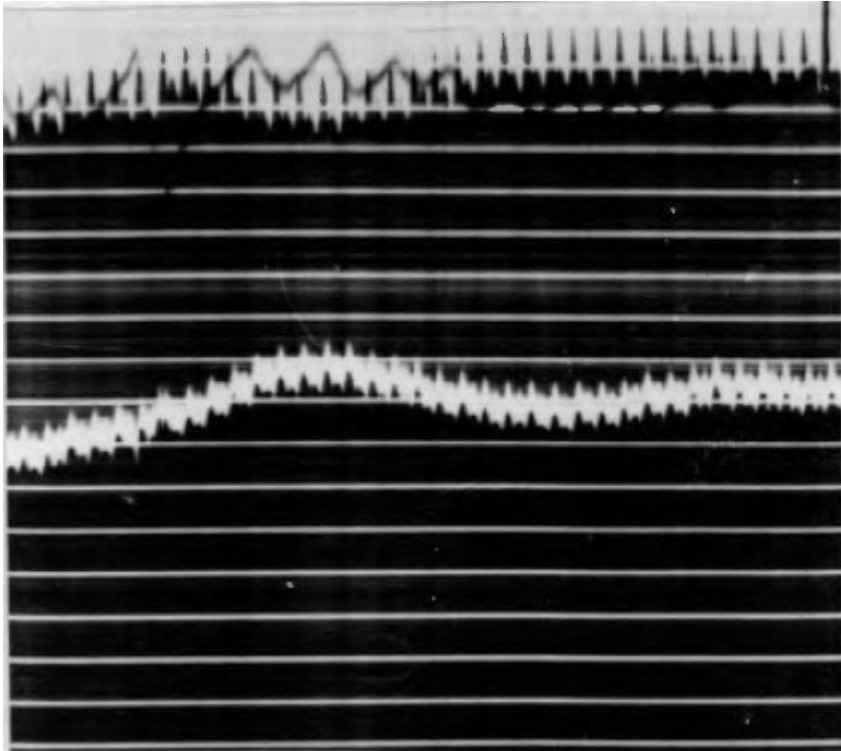


Fig. 11 (b) – Plethysmogram of the left index finger and left big toe. The subject used was the same in Fig. 11 (a). Both tracings were recorded during one experiment. Subject instructed to take a moderately deep breath. No vasoconstriction occurred.

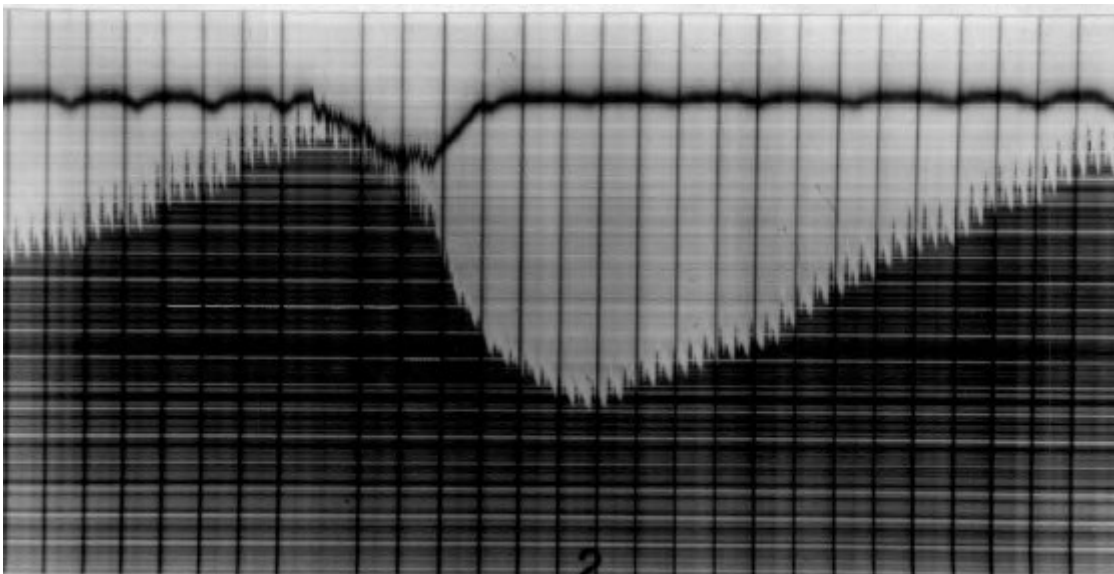


Fig. 12. Plethysmogram of the left index finger. Subject instructed to breathe rapidly and shallowly. Note the vasoconstriction.

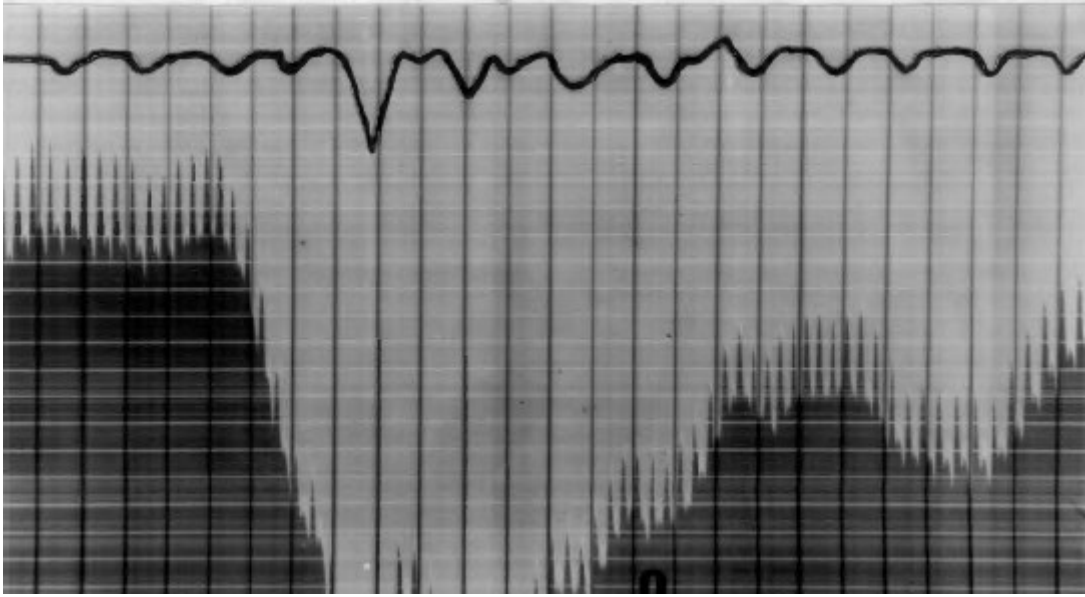


Fig. 13. Plethysmogram of left big toe. Subject instructed to attempt a deep breath against a closed glottis. Note the vasoconstriction and shift in the respiratory tracing indicating the extent of the chest expansion.

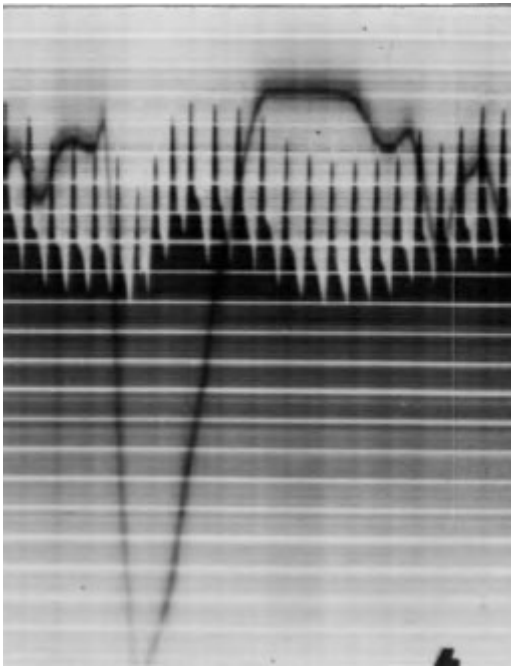


Fig. 14 (a) – Plethysmogram of the left big toe of a patient who had had a lumbar sympathectomy done a few weeks before the experiment. No vasoconstriction occurred with one deep breath.

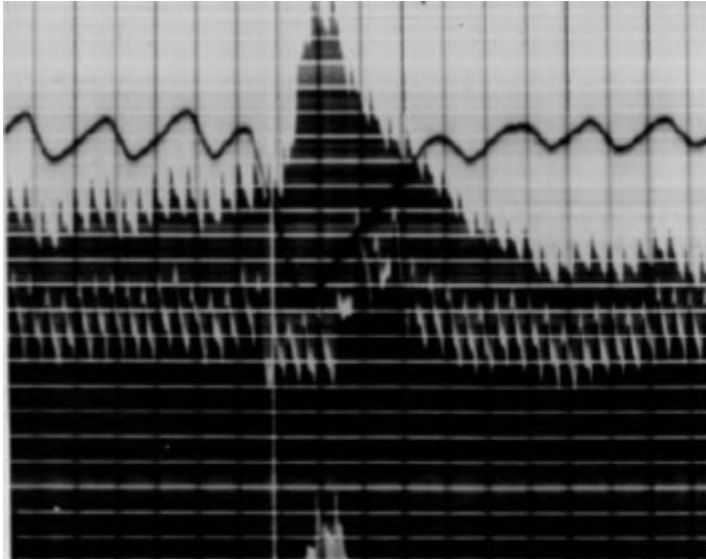


Fig. 14 (b) – Plethysmogram of the left index finger (upper tracing) and left big toe (lower tracing) of a patient who had had a lumbar sympathectomy several months before the experiment. He had no occlusive vascular disease. Note vasoconstriction occurs in the finger but not in the toe after one deep breath.

**TABLE 1**

The changes in pulse volume after a single deep breath in normal subjects and in hyperventilators.

Normal subjects	Normal pulse volume ml.	Pulse volume after 1 deep breath ml.	Duration of change in pulse volume. sec.	Normal respiratory rate. Breath/min.	Normal pulse rate. Beats/min.
L.	0.018	0.01	25	18	78
D.	0.012	0.007	20	24	72
M.	0.021	0.011	43	21	78
A.	0.012	0.006	25	12	72
P.	0.008	0.004	20	18	90
S.	0.025	0.012	60	24	72
WC.	0.013	0.005	20	20	72
C.	0.012	0.004	30	24	72
<b>AVERAGE</b>	<b>0.0151</b>	<b>0.0073</b>	<b>30.3</b>	<b>20.1</b>	<b>75.7</b>

Hyper-ventilators	Normal pulse volume ml.	Pulse volume after 1 deep breath ml.	Duration of change in pulse volume. sec.	Normal respiratory rate. Breath/min.	Normal pulse rate. Beats/min.
Wi.	0.006	0.003	25	21	78
A.	0.005	0.002	20	21	78
K.	0.01	0.005	12	18	78
B.	0.01	0.005	20	18	90
H.	0.005	0.003	20	24	78
R.	0.01	0.002	30	24	84
M.	0.011	0.005	35	18	66
N.	0.01	0.005	30	18	72
<b>AVERAGE</b>	<b>0.0083</b>	<b>0.0037</b>	<b>24</b>	<b>20.2</b>	<b>78</b>

## Comment

A reflex exists whose afferent path is not precisely known. The stimuli that trigger it are: the act of taking a breath of sufficient depth; the act of making an obstructed respiratory effort (where the movement of the chest is nearly as great as that in taking a deep breath); and a series of rapid, shallow breaths. The different path is by way of the sympathetic nerve fibers. The response is vasoconstriction which reduces peripheral pulse volume to less than half of its initial height and reduces the rate of arterial inflow. This peripheral vasoconstriction persists for an average of 30 seconds.

In normals and in hyperventilators the reflex vasoconstriction after a deep breath has the same characteristics. The only striking difference between the two groups is that the average hyperventilator has generally a smaller pulse volume than the normal subject so that any procedure that produces vasoconstriction causes a considerable reduction in peripheral blood flow.

## 2. The effect of 2 minutes of overbreathing

The time period of 2 minutes was chosen because previous experience had shown that some of the subjects developed tetanic spasms if they hyperventilated for longer. This broke the seal of the plethysmograph and interrupted the experiment.

Subjects were instructed to breathe deeply at a rate of 30 to 40 breaths per minute. A metronome was tried initially to regulate the rate exactly but was later abandoned because it introduced the factor of mental activity. The depth was not regulated because to achieve this too complicated a procedure is required.

The same subjects were used as those in the first series of experiments.

The table shows the results obtained and the graph illustrates some of the points. (Table 2, Fig. 15).

The normal controls finished their 2 minutes of hyperventilation with:

- (a) An average pulse volume of 0.0051 ml.
- (b) A persistence of this vasoconstriction for an average of 3.2 minutes.
- (c) An average pulse rate of 95 beats per minute.
- (d) A respiratory tracing that in six of eight cases was notable for periods of apnoea of several seconds duration.
- (e) A persistence of the abnormal respiratory rhythm for an average of 2.8 minutes.

The hyperventilators finished their 2 minutes of overbreathing with:

- (a) An average pulse volume of 0.0039 ml.
- (b) A persistence of this vasoconstriction for an average of 5.7 minutes.
- (c) An average pulse rate of 97 beats per minute.
- (d) A respiratory tracing that in only one case showed any evidence of apnoea and in some cases showed an increase in depth compared with the breathing before hyperventilation.
- (e) A persistence of the respiratory abnormality for an average of 3.7 minutes.

The hyperventilators after 2 minutes of overbreathing have a smaller peripheral blood flow than the normal controls. In addition, this vasoconstriction persists much longer. The interpretation of the

pathogenesis of the vasoconstriction after 2 minutes of overbreathing is more complicated than that following a single deep breath.

**TABLE 2**

The changes in pulse volume after 2 minutes of overbreathing in normal subjects and in hyperventilators

Normal controls	Pulse volume in ml.	Pulse rate	Respiratory rate and character	Persistence of respiratory abnormality (minutes)	Persistence of vasoconstriction (minutes)
L.	0.005	102	21 with no apnoeic periods	4	4
D.	0.006	90	12 with many apnoeic periods	2	3
M.	0.005	105	18 with apnoeic periods	2.5	4
A.	0.004	108	21 with apnoeic periods	3	3
P.	0.002	105	20 with apnoeic periods	3	4
S.	0.01	84	18 with numerous periods of apnoea	2.5	1.5
WC.	0.005	90	14 with numerous periods of apnoea	2.5	3.5
C.	0.006	78	20 with periods of apnoea	3	3
<b>AVERAGE</b>	<b>0.005</b>	<b>95.2</b>	<b>18 with 7 out of 8 showing apnoea</b>	<b>2.8</b>	<b>3.2</b>

Hyper-ventilators	Pulse volume in ml.	Pulse rate	Respiratory rate and character	Persistence of respiratory abnormality (minutes)	Persistence of vasoconstriction (minutes)
Wi.	0.004	96	15 with apnoeic periods	2.5	4
A.	0.0018	120	24-no apnoea	3.5	5.5
K.	0.003	102	15 with apnoeic periods	4	8
BX.	0.004	108	17-no apnoea	3	6.5
H.	0.003	96	30-no apnoea	7	10
R.	0.005	90	27-no apnoea, grossly irregular	4	3
M.	0.005	78	24-no apnoea	3	6
N.	0.004	90	24-no apnoea	3	3
<b>AVERAGE</b>	<b>0.009</b>	<b>97.5</b>	<b>23 with 2 out of 8 showing apnoea</b>	<b>3.7</b>	<b>5.7</b>

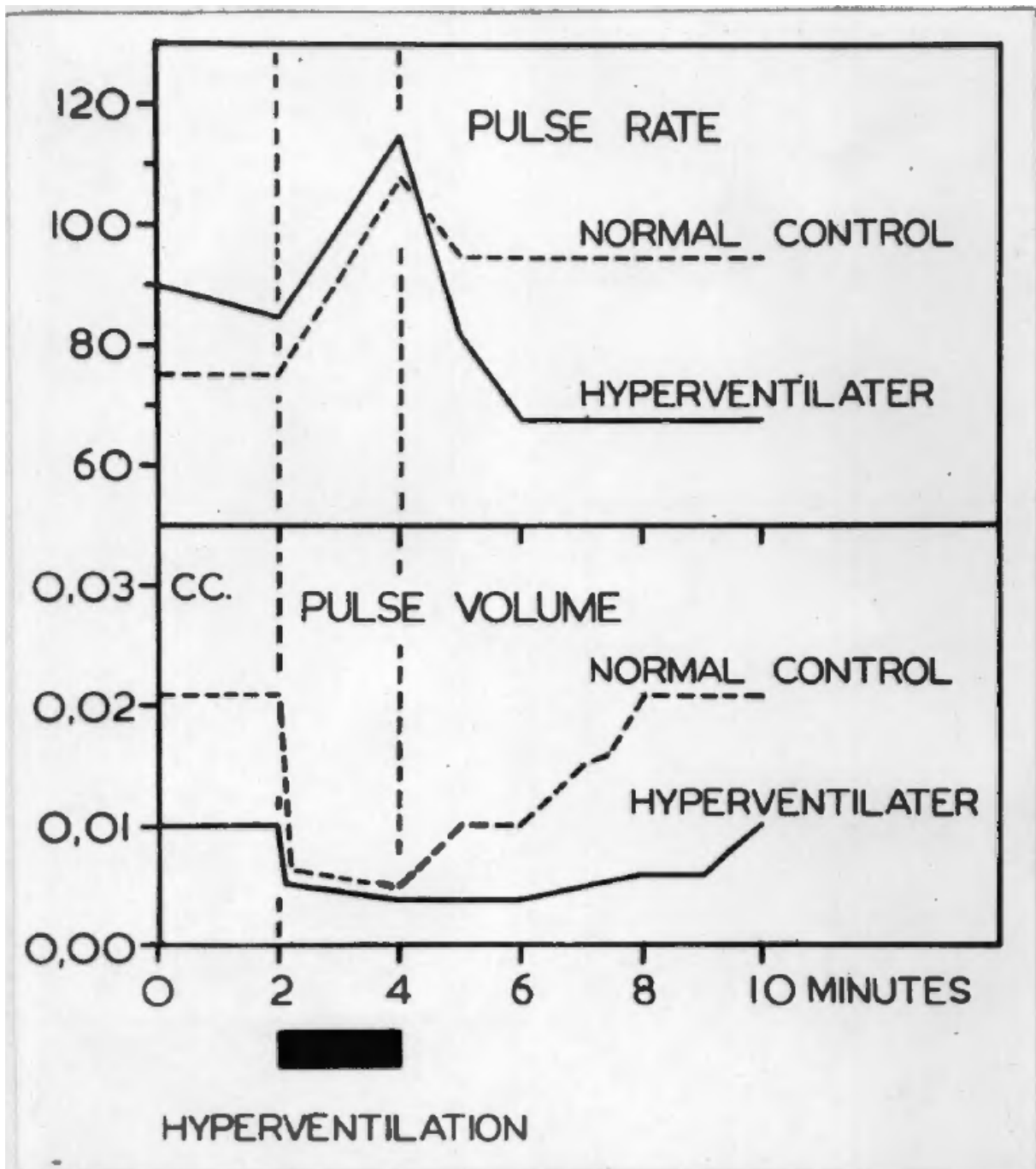


Fig. 15. This illustrates the change in pulse rate and pulse volume of a normal control and a hyperventilator after 2 minutes of overbreathing. Note the small initial pulse volume and the persistence of vasoconstriction in the hyperventilator.

**Two factors complicate the results:**

1. A circulatory factor, manifesting itself in tachycardia. Presumably, this results from the physical exertion of overbreathing.

In both the normal controls and the hyperventilators this increase varied between 6 and 30 beats per minute and persisted in both groups for about 1 minute. It cannot, therefore, be



invoked to explain any difference between the two groups as far as the degree and persistence of vasoconstriction are concerned.

It is, however, interesting to compare the response of a sympathectomized patient to the effects of the 2 minutes of overbreathing.

In this type of case, the reflex vasoconstriction in response to deep breathing does not occur because its motor path has been removed. A diminution in pulse volume nevertheless does occur and is correlated with the tachycardia. (Fig. 16 and 17).

2. The type of respiration after a period of hyperventilation is important.

Six of the normal controls showed a slowing of respiration due to many apnoeic pauses. (Fig.18).

This abnormality persisted for 2 to 3 minutes. The remaining two normal controls immediately resumed normal breathing but at a slightly slower rate.

Four of the hyperventilators continued to breathe much more deeply than before hyperventilation. (Fig. 19).

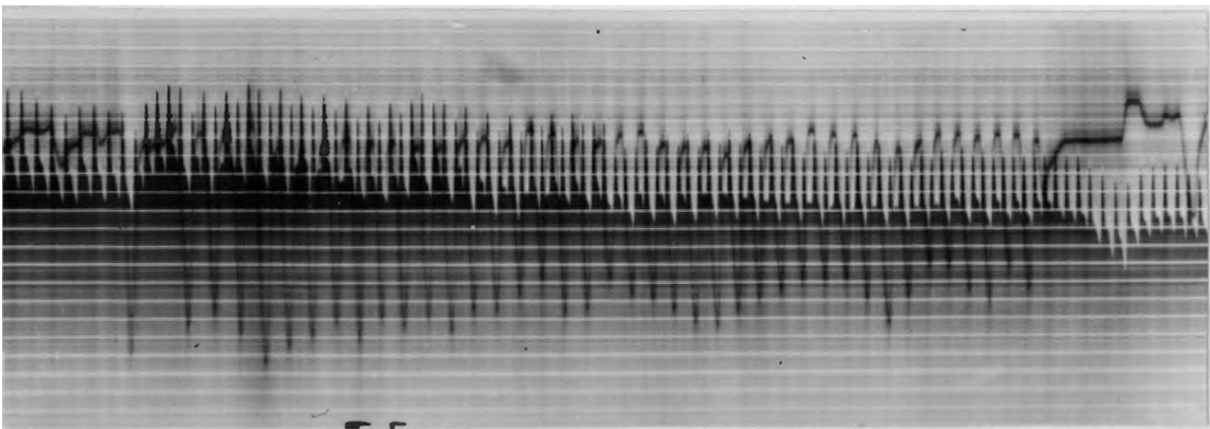


Fig. 16. Plethysmogram of the left big toe of a patient who had had a lumbar sympathectomy several months before this experiment. One minute of hyperventilation is illustrated. Note that a diminution in pulse volume occurs. This is due to the tachycardia.

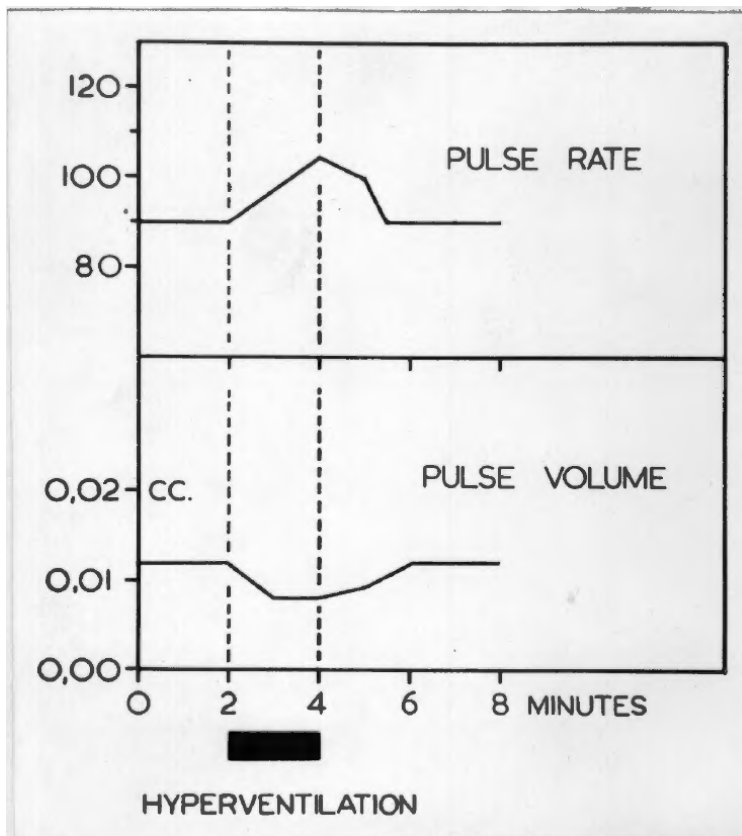


Fig. 17. This shows the correlation between change in digital pulse volume and change in pulse rate after 2 minutes of overbreathing in a patient in whom the sympathetic chain had been completely removed.

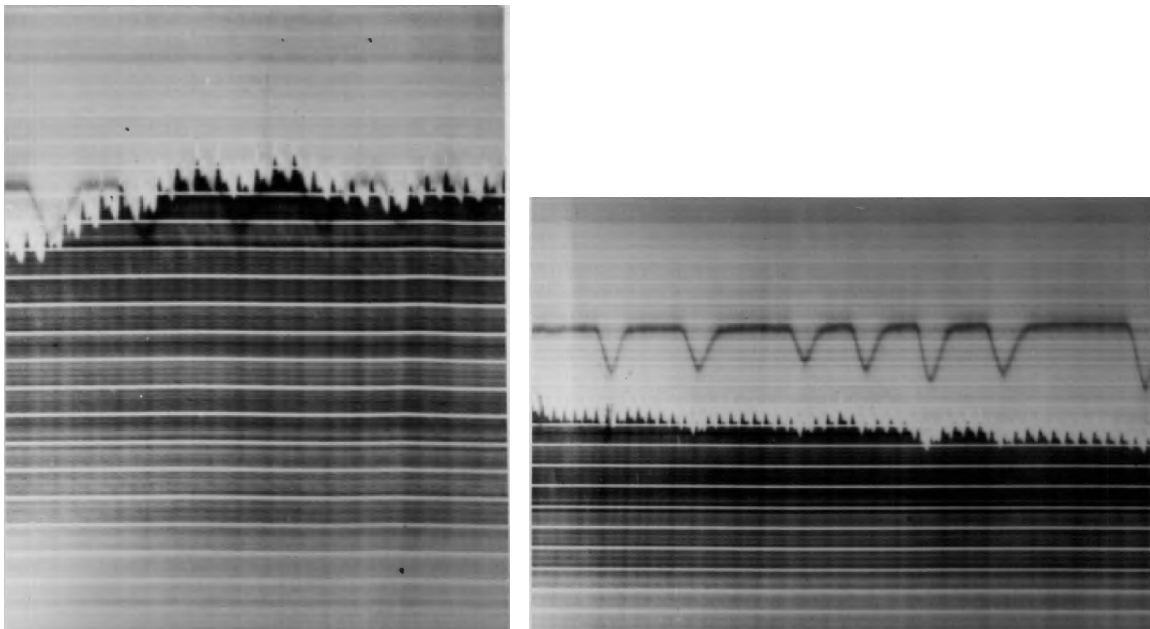


Fig. 18 (a) and (b) – Respiratory tracing of a normal subject:

- (a) before 2 minutes of hyperventilation.
- (b) and after 2 minutes of hyperventilation. Note apnoeic periods in (b).

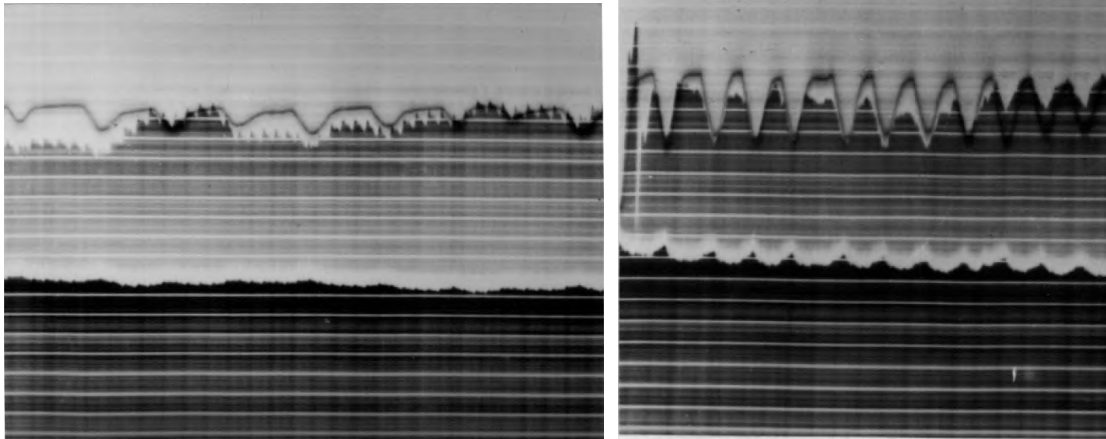


Fig. 19 (a) and (b). Respiratory tracing in a hyperventilator:

- (a) before 2 minutes of hyperventilation and
- (b) after 2 minutes of hyperventilation.

One patient showed grossly irregular respiration with many periodic deep breaths and spells of rapid, shallow breathing.

Two patients resumed normal breathing but at a slightly slower rate.

Only one patient showed any apnoea and he spontaneously remarked that he had consciously held his breath after the experiment because the whole mechanism of hyperventilation with its consequent physiological changes had been previously explained to him.

The respiratory abnormality in the hyperventilators persisted for 3 to 4 minutes.

It is obvious that the first five hyperventilators would tend to remain in a state of vasoconstriction longer than the normal controls by virtue of the increased depth of their breathing, or periodic deep breaths.

The remaining three patients had, however, no respiratory cause for a lengthy persistence of vasoconstriction after hyperventilation. Two of these cases had a vasoconstriction that lasted 6 and 8 minutes respectively. This may be due to a more rigid vasomotor tone than in normal subjects.

### 3. The effect of hyperventilation:

- (a) In ten normal controls with one hand warm and the other cool.
- (b) In ten normal controls with the limbs elevated.
- (c) In two patients at varying intervals after a two-stage sympathectomy of the upper limbs.

(a) Ten normal controls free of any organic vascular disease were used for this experiment.

Both hands were simultaneously immersed in water – one hand at a temperature of 57°F and the other at a temperature of 110°F. If the water is made too hot or too cold the subjects experienced discomfort in the hands which interfered with their accurate observation of the paraesthesia resulting from hyperventilation.

The hands were immersed for 1 1/2 minutes. They were then dried by the experimenter. The subject was then seated comfortably with the hands resting lightly on a table. Care was taken to ensure that there was no pressure on peripheral nerves. The subject then began to hyperventilate at a rate of about 35 breaths per minute. The time and place in which paresthesia manifested themselves were noted. The experiment was repeated the following day with the hands interchanged. (Table 3).

It was found that if the experiment was repeated too soon – that is some hours later – the hand in which paresthesia had been most intense during the first experiment always tingled first in the second experiment. It appears that the irritability of the peripheral nerve induced by overbreathing may persist for a considerable time – certainly several hours.

**TABLE 3**

Times of onset of paresthesia in ten subjects who were instructed to hyperventilate with one hand cooled and the other warmed. The hand that was initially cooled is put first.

Subject	Cold hand	Results during hyperventilation
I.	Left	After 2 minutes left hand began tingling. After 5 minutes no tingling in the right hand but cerebral discomfort so marked that the experiment was stopped.
	Right	After 2 minutes right hand began tingling. After 4 minutes no tingling in the left hand.
V.	Right	After 4 minutes right hand began tingling. After 5 minutes left hand began tingling.
	Left	After 3 minutes left hand began tingling. After 4 minutes right hand began tingling.
L.	Right	After 2 minutes right hand began tingling. After 3 1/2 minutes, the left hand began tingling.
	Left	After 2 minutes left hand began tingling. After 5 minutes no tingling in the right hand.
S.	Left	After 1 minute left hand began tingling. After 3 1/2 minutes, the right hand began tingling.
	Right	After 2 minutes right hand began tingling. After 3 minutes left hand began tingling.
M.	Right	After 1 1/2 minutes, the right hand began tingling. After 2 1/2 minutes left hand began tingling.
	Left	After 1 1/2 minutes left hand began tingling. After 2 1/2 minutes, the right hand began tingling.
D.	Left	After 3 minutes left hand began tingling. After 3 1/2 minutes, the right hand began tingling.
	Right	After 4 minutes right hand began tingling. After 5 minutes left hand began tingling.
A.	Right	After 2 minutes right hand began tingling. After 2 1/2 minutes left hand began tingling.

	Left	After 1 1/2 minutes left hand began tingling. After 2 minutes right hand began tingling.
M.	Left	Bilateral tingling more intense in the left hand.
	Right	Bilateral tingling equally intense in both hands.
L.	Left	After 2 minutes left hand began tingling. After 3 ½ minutes, the right hand began tingling.
	Right	After 2 minutes left hand began tingling. After 3 minutes right hand began tingling.
W.	Left	After 1 minute right hand began tingling. After 2 minutes left hand began tingling.
	Right	After 2 minutes right hand began tingling. After 3 minutes left hand began tingling.

From Table 3 it can be seen that in seven of the ten subjects hyperventilation resulted in paraesthesia in the cold hand first – whether that hand was the right or the left. In one subject the temperature of the hands did not seem to make any difference as he developed paresthesia simultaneously in both the cold and warm hand, after overbreathing for a few minutes. In one subject paresthesia always appeared first in the left hand, whether it, was warm or cool. In one subject paresthesia always appeared first in the right hand whether it was warm or cool.

### Comment

It seems therefore that in most people local cooling of a hand will hasten the appearance in that hand of the paraesthesia resulting from overbreathing.

Two of the subjects were right and left-handed dominant as far as the onset of paresthesia was concerned. The point has already been mentioned in the clinical section that in some people the site of the initial tingling is always the same. This local susceptibility does not seem to depend on any vascular factor and it is apparently strong enough to overrule any temperature differences.

### (b) The effect of hyperventilation in elevated limbs.

Ten normal controls free of any organic vascular disease were used for this experiment. The subject lay on the floor with the head on a pillow. One leg was extended and the other elevated at an angle of about 75 degrees. The heel rested against the side of a padded couch. One arm was supported by the observer without compressing any peripheral nerves. The other arm was extended at the side of the subject. This posture was maintained for 2 minutes to accustom the subject to it. The subject then began to overbreathe and reported on the development of paresthesia.

**TABLE 4**

Times of onset of paresthesia in ten subjects who were instructed to hyperventilate while one leg and one arm were kept elevated.

Subject	Limb elevated	Results during hyperventilation
---------	---------------	---------------------------------

I.	Left leg	After 1 minute tingling began in the left leg.
	Right arm	After 2 minutes tingling began in the right arm. After 4 minutes tingling began in the right leg.
S.	Left leg	After 5 minutes tingling began in the left leg.
	Right arm	After 6 minutes tingling began in the right arm.
D.	Left leg	After 1 minute tingling began in the left leg.
	Right arm	After 3 minutes no tingling anywhere else. Cerebral symptoms so marked that refused to continue overbreathing.
W.	Left leg	After 2 minutes tingling began in the left leg.
	Right arm	After 4 minutes tingling began in the right arm.
V.	Right leg	After 3 minutes tingling began in the right leg.
	Left arm	After 4 minutes tingling began in the left leg.
M.	Right leg	After 2 minutes tingling began in the right leg. After 3 minutes tingling began in the left leg.
	Left arm	After 3 1/2 minutes tingling began in the left arm. After 5 minutes tingling began in the right arm.
LO.	Right leg	After 3 minutes tingling both hands. No paresthesia in feet.
	Left arm	After 5 minutes too uncomfortable to continue.
A.	Left leg	After 3 minutes tingling began in the left leg.
	Right arm	Subject too uncomfortable to continue overbreathing.
T.	Right leg	After 2 minutes tingling began in the right arm.
	Left arm	After 3 minutes tingling began in the right leg. Subject too uncomfortable to continue overbreathing.
M.	Right leg	After 2 minutes tingling began in the right leg.
	Left arm	After 3 minutes tingling began in both hands. After 4 minutes tingling began in the left leg.

From Table 4 it can be seen that in eight subjects paresthesia first became manifest in the elevated leg; in one subject in both hands; and in one subject in the non-elevated arm. In no subject did the elevated arm tingle first though in three cases it took second place to the elevated leg. Four subjects were unable to complete the experiment despite their recumbent attitude. They found the unnatural position of the limbs too trying when allied with the usual unpleasant symptoms of hyperventilation.

#### **Comment**

Elevation of the leg hastens the onset of the paraesthesia resulting from hyperventilation. This is remarkable because normally with the subject recumbent the legs are often late in manifesting paresthesia.

(c) The effect of hyperventilation in two patients at varying intervals after a two-stage sympathectomy of the upper limbs.

This patient was a European female of 20 years who suffered from acrocyanosis. She was an excellent witness. The experiment was performed 5, 7, 13, and 24 days after the right arm had been adequately sympathectomized.

(i) After 5 days:

The right arm was warm and dry, the left cold and blue.

The patient lay recumbent and began to overbreathe at about 35 breaths per minute. She was told to report any unusual sensations immediately. She reported as follows:

- After 2 minutes: tingling in right hand;
- 3 minutes: coldness in left hand;
- 4 minutes: the whole right arm tingling markedly;
- 5 minutes: jaw tingling;
- 10 minutes: tingling started in left hand;
- 15 minutes: right arm felt numb and "dead".
- 25 minutes: subjective stiffness of the right hand and adduction of the thumb – commencing tetanic spasm. At this time there was only slight tingling in the left hand.

Throughout the experiment, the right hand remained warm and dry while the left hand became progressively colder and sweated profusely.

(ii) After 7 days:

The experiment was repeated. The patient reported:

- After 2 minutes: dizziness;
- 3 minutes: tingling in right hand;
- 4 minutes: tingling in legs;
- 6 minutes: slight tingling in the left hand. (At this stage the patient began to yawn uncontrollably and continued to do so till the end of the experiment.)
- 9 minutes: a lame, tingling feeling in the whole of the right arm and still slight tingling in the left hand;
- 15 minutes: tingling increased in left hand;
- 17 minutes: tetanic spasm commenced in the right hand.

(Throughout the experiment the right hand remained warm and dry while the left hand became progressively colder and sweated profusely).

(iii) After 13 days (and 5 days after the left arm had been sympathectomized): at this time both hands were warm and dry. The patient had some slight tingling in the left ulnar distribution, probably the result of traction on the brachial plexus during the second operation.

She reported:

- After 1 minute: dizziness;
- 3 minutes: both hands tingling;
- 5 minutes: both legs tingling;

- 6 minutes: uncontrollable yawning;
- 7 minutes: her whole body twitching;
- 12 minutes: continued to yawn and felt sleepy.
- 13 minutes: the whole of left arm tingle much more markedly than the right side;
- 16 minutes: left arm felt “*very funny – sort of lame and tingly*”.
- 20 minutes: left arm still tingled markedly, a little tingling of the right hand.

(iv) After 24 days (and 17 days after the left arm had been sympathectomized): at this time both hands were warm and dry and the slight tingling in the ulnar distribution had diminished. The patient breathed at 40 breaths per minute – reasonably deeply.

She reported:

- After 3 minutes: dizziness;
- 4 minutes: pain in chest;
- 5 minutes: slight tingling in both hands – more intense in left ulnar nerve distribution;
- 10 minutes: generalized shivering and feet felt very cold;
- 11 minutes: slight tingling in both forearms;
- 16 minutes: both legs tingling;
- 18 minutes: both arms felt “*dead*”;
- 26 minutes: both arms tingling and legs felt “*dead*”;
- 28 minutes: hands and feet tingling markedly and fingers “*stiff*”;
- 44 minutes: tingling sensation wore off in hands, except in the left ulnar nerve area, legs still tingling slightly and feet cold and sweating, face and ears tingling markedly. She remarked that the tingling was much less than on previous occasions. There was no motor spasm throughout the experiment.

**Comment:**

The first two tests were carried out 5 days and 7 days after the right arm had been sympathectomized. Twenty minutes of overbreathing resulted in the appearance of tetanic spasm in the right hand with moderate paresthesia in the left hand.

The third test was carried out 13 days after the right and 6 days after the left arm had been sympathectomized. On this occasion, the left hand developed marked paresthesia with minimal tingling in the right hand.

The fourth test was carried out 24 days after the right and 17 days after the left arm had been sympathectomized. On this occasion paresthesia of moderate-intensity developed in both hands. This wore off later despite continued hyperventilation and never progressed to tetanic spasm.

In other words, the subject with an established sympathectomy was much less susceptible to the manifestations of peripheral nerve irritability resulting from hyperventilation than is a normal subject. Forty-four minutes of reasonably vigorous hyperventilation in a normal subject will almost certainly produce a well-marked tetanic spasm in the arms.

The transient increase in susceptibility of the sympathectomized limbs a few days after the operation could be explained by postulating a temporary irritability of the peripheral nerves as a result of traction on the brachial plexus at operation. This does occur and did so in this case because the patient had symptoms of left ulnar nerve irritation.



2. This was a European female of 28 years who was suffering from acrocyanosis.

(i) The first experiment was done preoperatively. The patient was very apprehensive. She reported as follows:

1. After 1 minute of overbreathing: markedly dizzy;
2. 3 minutes: felt cold (her whole body began to shiver);
3. 7 minutes: tingling in both hands – much more intense on the left side.

She refused to continue hyperventilation.

Her hands at the onset of the experiment had been blue and cold and became progressively colder and sweated profusely.

(ii) Experiment is repeated 11 days after the left arm had been sympathectomized. She did not have Horner's syndrome. The left hand was warm and dry and the right cold and blue.

She began to hyperventilate at 36 breaths per minute and flexed her legs because she could "*breathe better*".

4. After 2 minutes: giddiness;
5. 5 minutes: Tingling began in right hand;
6. 6 minutes: her teeth began chattering but she said she was not very cold;
7. 11 minutes: "*lameness*" in the left hand – but no tingling;
8. 14 minutes: right hand tingling markedly;
9. 16 minutes: feet began to tingle;
10. 21 minutes: right arm and both feet tingling markedly;
11. 24 minutes: right hand stiff and felt "*terrible*".
12. 26 minutes: tetanic spasm right hand. At this time the left hand felt normal apart from slight "*lameness*".

20 days after the left arm had been sympathectomized and 6 days after the right arm had been sympathectomized:

13. After 3 minutes: dizziness;
14. 6 minutes: both feet tingling markedly;
15. 7 minutes: generalized shivering;
16. 9 minutes: slight laryngeal stridor;
17. 11 minutes: marked stridor – became extremely anxious and semi-conscious with thrashing around of her limbs. The experiment was stopped.

**Comment:**

This woman differed from the previous patient in that the sympathectomy was not so extensive – she did not develop Horner's syndrome as the stellate was not completely removed.

Before her operation hyperventilation results in paraesthesia in both hands – more markers on the left side. Eleven days after the left arm had been sympathectomized 26 minutes of hyperventilation resulted in a tetanic spasm of the right hand and paresthesia in the legs. In the left hand, there was only slight "*lameness*".

Twenty days after the left arm had been sympathectomized and 6 days after the right arm had been sympathectomized 11 minutes of overbreathing resulted in paresthesia in both feet but no change in the hands. The laryngeal stridor terminated the experiment.

A comparison of her reactions before and after sympathectomy shows that the operation made her upper limbs less vulnerable to the peripheral nerve signs resulting from hyperventilation. She did not show the transient increase in susceptibility that the first case showed. This can be attributed to the fact that the operation, being less extensive, did not interfere with the brachial plexus.

## CHAPTER 7 – DISCUSSION

It has become evident that a great deal of illness is of emotional origin and that all illness has its emotional component.

The hyperventilation syndrome is one of the ways in which emotional stress becomes manifest. An attempt has been made to study, not only the clinical manifestations but also some of the physiological mechanisms invoked by overbreathing. It is felt that an understanding of the physiological background of an emotionally engendered illness will lead to a much clearer conception of the, at present, vaguely understood entity of "*psychosomatic medicine*".

Hyperventilation results from a stimulus to the respiratory center. The manner in which this stimulation is brought about is not precisely known but it is in some way connected with stress.

The purpose of the hyperventilation is a preparation for motor activity. Symptoms result when this motor activity is restrained by the inbuilt social and cultural inhibitions of the individual. The remarks of Russel (1952) on experimental neuroses are pertinent here. He says: "*The precipitating factor is conflict, but another essential factor present in all the successful experimental techniques, is restraint of voluntary movements, either by a harness or by the subject's own learned patterns of movement*".

It is interesting that most patients in this series found that they were unable to keep still during hyperventilation and that even purposeless movements relieved their symptoms to some extent. But, in the absence of coordinated motor activity, the main effect of the overbreathing was turned back on the body, causing a physical disturbance. This physical dysfunction was manifested in all systems of the body, but neurogenic dysfunction gives the hyperventilation syndrome its specific stamp.

Most of the patients were aware of respiratory dysfunction, but not that they were hyperventilating. The commonest complaint was that of not being able to get a satisfactory breath and this referred particularly to the depth of the breath. This respiratory difficulty is characteristically unrelated to exertion.

Once hyperventilation was established, the commonest group of symptoms were those of central nervous system disturbance. These comprised cerebral disturbances which, though rarely gross enough to result in loss of consciousness, were nevertheless distressing to the patient. They comprised dizziness, visual disturbance, feelings of unreality, etc. They may be associated with electroencephalographic changes. There is a reduction in cerebral blood flow of about 30%.

Peripheral nerve involvement was manifested by paresthesia, starting in hands and feet and later becoming generalized. A few cases progressed to tetanic spasm.

The commonest gastrointestinal disturbance was distension of the stomach which resulted from air-swallowing during overbreathing.

Circulatory disturbances comprised precordial pain, palpitation, and coldness of the extremities. Two patients complained of diuresis. Fatigue was a common symptom.

The signs and symptoms were enhanced if the patient was emotionally disturbed, in fact if stress was present.

At least three separate physiological mechanisms are invoked as a direct result of overbreathing.

These are:

1. An increased alkalinity of the blood.
2. A reflex peripheral vasoconstriction.
3. Circulatory effects resulting from the muscular exercise of overbreathing.

1. The increased alkalinity of the blood which results from loss of CO<sub>2</sub> during hyperventilation is of primary importance. Patients who overbreathe a CO<sub>2</sub>-rich mixture do not develop the characteristic symptoms of neurogenic dysfunction. Conversely, many of the symptoms of this syndrome are rapidly relieved by re-breathing CO<sub>2</sub>. It is the alkalosis that:

- (a) Increases neuromuscular irritability to the point where tetany may develop.
- (b) Causes cerebral blood vessels to constrict. This conserves their low CO<sub>2</sub> content.
- (c) Renders hemoglobin reluctant to part with its oxygen thereby interfering further with the nutrition of the tissues and especially of nerve tissue.

2. Reflex peripheral vasoconstriction is an integral part of hyperventilation syndrome.

It accounts for the cold extremities, the seating, and the pallor. To Henderson (1909) these features were so striking that he described at length the "*shock-like*" state seen after prolonged overbreathing.

It has been shown that the motor route for this reflex is along the sympathetic nerve fibers. The afferent path is not precisely known but seems to be connected in some way with the expansion of the chest or lungs. The vasoconstriction after several minutes of overbreathing persists for many minutes and tends to persist longer in hyperventilators. This can be only partially explained by the type of respiration after hyperventilation in these subjects, and an additional factor, which is a less easy adaptability of their vasomotor tone, has been suggested.

If hyperventilation is assumed to be part of the physiological preparation for flight or attack, what is the significance of the reflex peripheral vasoconstriction? It seems reasonable to assume that, like the effect of adrenaline, it is part of a general vascular shift to supply the skeletal muscles with additional blood. Limb plethysmography is notoriously difficult to interpret, as so many tissues are included in the plethysmograph that it becomes difficult to assign to any one tissue any specific change in blood supply. With the digital plethysmograph, one is, for all practical purposes, dealing only with skin. Eichna and Wilkins (1941) studied the changes in the volume of the forearm and calf after various stimuli which are known to produce skin vasoconstriction, e.g. deep breath, noise, mental activity, etc. By far the commonest response was a moderate decrease in limb volume. Occasionally the limb increased in volume, either moderately or markedly.

We know that with one deep breath a marked skin vasoconstriction is produced. If the limb as a whole usually shows only a moderate decrease in volume and occasionally even an increase in volume, it seems reasonable to assume that the relatively large quantity of blood being diverted from the skin is being accommodated elsewhere in the limb and that it is probably muscle tissue which is receiving the extra blood.

Clarke (1952) claimed that during moderate over-ventilation (20 per minute for 3 minutes at maximum depth) there is a two-fold increase in blood flow to the forearm. He attributed this to vasodilatation in the muscles and thought that it resulted from the hypocapnia.

The next question that arises is whether this assumed redistribution of blood in the limbs during overbreathing plays any part in the genesis of the peripheral neurological symptoms and signs of the hyperventilation syndrome? Evidence that it plays some part is the fact that procedures designed to interfere with the normal reflex distribution of blood with overbreathing can alter the speed of development and the intensity of the manifestations of peripheral nerve irritability.

Cooling a hand or elevating a limb, especially the leg, usually accelerates the onset of paresthesia, whereas sympathectomizing a limb has the opposite effect.

Cooling a hand presumably increased the intensity of the reflex peripheral vasoconstriction. The effect of elevating a limb is more complicated as shown by Gootz in 1950. He demonstrated striking alterations in the vascular supply to a limb during elevation.

These are:

1. An increase in the systolic elevation and a decrease in the dicrotic wave of the pulse.
2. An accentuation of the changes in digital volume resulting from extrinsic stimuli, e.g. noise, deep breath, etc.
3. A delayed response to reflex body heating.
4. A drop in skin temperature.

These changes were attributed to an acceleration of the venous return from the limb. They are more marked in the legs because the venous return from the legs is considerable.

The acceleration of the onset of paresthesia with elevation is probably due to the fact that all the tissues in the limb have a less effective blood supply during elevation because of the rapidity of the venous return.

Removal of the sympathetic supply to a limb abolishes the reflex peripheral vasoconstriction of deep breathing. In two cases of upper limb sympathectomy, the paraesthesia of hyperventilation was tardy in appearing and much less intense once the sympathectomy had become established. This effect was strikingly illustrated in one case where the opportunity arose of recording the patient's response to overbreathing pre-operatively.

The next question and this can only be dealt with very speculatively, is how precisely this vascular factor works.

We know that a reflex peripheral vasoconstriction of the skin occurs. This will interfere with the vascular supply of the nerve terminal. But the crucial question appears to be whether there is a change in vascular supply to the peripheral nerve itself. This is not known at present, but if the general vascular shift in the limb is to supply the skeletal muscles, then the peripheral nerve may suffer with the skin in depletion of its blood supply.

Ischemia itself is a potent agent in increasing the irritability of peripheral nerves. Lewis, Pickering, and Rothschild (1933) demonstrated this, and the generally accepted explanation of the Trousseau phenomenon is that it activates the nerve through ischemia. (Lewis, 1942). Neuromuscular tissue functions less well when cold, e.g. myotonic spasm is often precipitated by cold.

It is the alkalosis that is of primary importance in the pathogenesis of the peripheral nerve irritability. This is emphasized by the fact that after 2 minutes of overbreathing, although the vasoconstriction persists for about 3 minutes, the paresthesias disappear in about a minute. Nevertheless, these investigations indicate that the peripheral vasoconstriction does in some way lower the threshold of nerve irritability, and so contributes to the manifestations of the hyperventilation syndrome. The factor of ischemia may also be of importance, in the genesis of the tetany of hypocalcemic patients. One case of this (resulting from steatorrhoea) was seen and she spontaneously remarked that cold precipitated many of her attacks and she could often avert an impending attack by warming her limbs.

3. The effect of overbreathing purely as a form of muscular exercise is another factor of importance. This has only been touched on. All patients who overbreathed for 2 minutes developed an increase of heart rate ranging from 6 to 30 beats per minute. This lasted for about 1 minute after the cessation of overbreathing. One patient in the series, who presented with "*palpitations*" as her major complaint, regularly produced a pulse rate of 120 beats per minute after a few minutes of overbreathing. This tachycardia also occurs in sympathectomized patients after hyperventilation and explains the diminution in pulse volume which develops despite the absence of reflex peripheral vasoconstriction.

A fourth factor that must receive mention because of the role of stress in the hyperventilation syndrome is the factor of adrenaline release. Although its direct study is outside the scope of this thesis it must be considered as a possible background factor because of its action as a respiratory stimulant; its effect in causing skin vasoconstriction and muscle vasodilatation and its influence in upsetting the ionic equilibrium. Although adrenaline release does not appear to alter the symptoms and signs of the hyperventilation syndrome in a qualitative sense; it probably plays a part in enhancing or maintaining the physiological effects of the other 3 factors.

Although the factors of alkalosis, reflex peripheral vasoconstriction, and circulatory effects from muscular effort and adrenaline release are separate and distinct they are intricately interwoven to produce a highly specific clinical picture which we recognize as the hyperventilation syndrome.

## **CHAPTER 8 – SUMMARY AND CONCLUSIONS**

1. A study has been made of the hyperventilation syndrome, the name given to a group of symptoms and signs which result from overbreathing.

In this thesis, the viewpoint has been taken that the hyperventilation is a physiological preparation for fight or flight. Certainly, emotional stress is responsible for most cases of the syndrome. Physical function rises because the patient, physiologically prepared for some form of motor activity, is inhibited by social or cultural traditions from carrying his emotional response over into a motor response.

2. The literature on the effects of overbreathing in man has been reviewed.

3. The clinical symptoms of forty patients with this syndrome have been analyzed. Neurogenic dysfunction, both central and peripheral, gives the syndrome its distinctive character but the involvement of other systems, especially the circulatory one, is often prominent.
4. The criteria for diagnosis, the value of a hyperventilation test, and differential diagnosis have been discussed.
5. Treatment consists of explaining the mechanism of hyperventilation to the patient, demonstrating the reproduction of symptoms by overbreathing and the relief of symptoms by re-breathing a carbon dioxide-rich atmosphere or by breath-holding. The idea is to break at one point the physiological chain of reactions of the emotional response.

Long-term treatment is aimed at relieving emotional stress by discussions with the patient and by teaching him the technique of progressive relaxation.

6. The experimental section inquires into the peripheral vasoconstrictor effect of overbreathing. This is an integral part of the syndrome.

The peripheral vasoconstriction is reflex and mediated through the sympathetic pathway. The afferent path is not precisely known but it is evoked by the act of taking a deep breath, making an obstructed respiratory effort, or by rapid, shallow breathing. It occurs with a carbon dioxide-rich mixture as well as with air or other gases. The reduction in pulse volume is considerable. Digital volume and arterial inflow are also reduced.

7. Plethysmographic studies of eight normal controls and eight members of the series of cases described show that this reflex peripheral vasoconstriction has the same characters in both groups.

The only difference between them is that the hyperventilators tend, clinically and plethysmographically, to be cold-handed, so that any vasoconstrictor stimulus will reduce their peripheral blood flow to a lower level than that of a normal subject responding to the same stimulus.

8. The following changes produced by 2 minutes of overbreathing have been investigated in eight normals and eight hyperventilators.
  - a. Reflex peripheral vasoconstriction.

In normal subjects, this vasoconstriction persisted for about 3 minutes after termination of 2 minutes of overbreathing. In the hyperventilators, the vasoconstriction persisted for about 5 minutes. The high vasomotor tone of the hyperventilators might be partly responsible for the longer duration of the vasoconstriction.
  - b. An increase in pulse rate.

This varied markedly in both normal subjects and hyperventilators. The range of increase was from 6 to 30 beats per minute. This increase in pulse rate also occurred

in sympathectomized patients. It caused a diminution in their pulse volume after 2 or more minutes of overbreathing.

c. Abnormal respiration.

In six of the eight normal subjects, the respiration after 2 minutes of hyperventilation was characterized by periods of apnoea. In the hyperventilators apnoea occurred in only one case; in four cases the respiration actually increased in depth compared with that before hyperventilation; in one case it was grossly irregular.

9. Investigations were undertaken to see whether the time of onset and intensity of the symptoms of peripheral nerve irritation was influenced by changes in the vascular supply to the limbs. The maneuvers carried out for this purpose were:

a. Cooling one hand and warming the other.

In seven of ten cases, local cooling accelerated the onset of paresthesia.

b. Elevating a limb.

This accelerated the onset of paresthesia in the leg in eight of ten cases.

c. Sympathectomized upper limbs.

Sympathectomy delayed the onset and diminished the intensity of paresthesia in both the cases investigated.

10. The syndrome is discussed with particular reference to the mechanisms brought into operation by overbreathing. These are:

a. An alkalemia produced by the blowing off of CO<sub>2</sub>. This produces a cerebral vasoconstriction, reducing blood flow in the brain by as much as 30 percent. It causes peripheral nerve irritability which manifests itself as tetany. It also interferes with tissue oxidation.

b. A reflex peripheral vasoconstriction which is responsible for the cold hands, sweating, etc. It is considered as part of a general vascular shift to supply the skeletal muscles with more blood. It is assumed that the peripheral nerve, as well as the skin, has its blood supply curtailed.

Consequently, the peripheral nerve is not only subjected to the exciting influence of the alkalosis but this excitation is enhanced by the ischemia resulting from the reflex peripheral vasoconstriction.

Maneuvers that accentuate this ischemia, such as local cooling or elevation of a limb, accelerate the onset of symptoms of peripheral nerve irritation. Conversely, sympathectomy, which abolishes the reflex peripheral vasoconstriction, delays the onset of these symptoms. It is pointed out that after several minutes of hyperventilation the peripheral pulse volume in sympathectomized limbs is also ultimately reduced. This diminution in pulse volume is closely correlated with the tachycardia that occurs after overbreathing.

c. Circulatory effects produced by the muscular exercise of overbreathing. Most patients get an increase in heart rate after several minutes of overbreathing. This varies widely between 6 and 30 beats per minute. In some patients who get a considerable increase in heart rate, "*palpitations*" is a major complaint. Fatigue, which is a very common complaint, is probably partly caused by the muscular work of overbreathing.

- d. There may be a background factor of emotional stress which, when present, enhances the symptoms and signs.

## CHAPTER 9 – APPENDIX OF CASE HISTORIES

This appendix summarizes forty cases individually. In all of them, except case 20, the symptoms and signs were reproduced by hyperventilation. Case 20 was too apprehensive to risk precipitating laryngeal stridor by overbreathing.

Case 18 is given in more detail than the others, not only because it is so representative of the syndrome but because the patient was an extremely reliable and intelligent observer.

18. E.M. stands for European male.
19. E.F. stands for European female.
20. C.M. stands for Colored male.
21. C.F. stands for Colored female.

### 1. J.N. – 36 years (E.M.)

This patient was an epileptic. He said that for about 2 years he had been rather worried because of his epileptic attacks and because of domestic tension. During this period he often got the feeling *“as though his chest had closed in”* and he felt compelled to rush out of the house to get fresh air. These attacks lasted about 10 minutes.

One week before coming to the hospital he got this feeling of not getting enough air. It was so acute that he actually tore his collar open *“to let in the air”*. He then became very dizzy and staggered like a drunk man clutching a fence to keep on his feet. He was not conscious of any paresthesia. This attack lasted about 45 minutes.

Three weeks later he reported back to out-patients to say that he had started to get an attack like his previous one but had immediately breathed into his hat and within a few minutes all his symptoms had disappeared.

### 2. S.B. – 42 years. (E.F.)

The patient stated that she was perfectly well until 6 months before our interview. One night, while preparing for bed, she developed a *“funny feeling over my heart as though something had stopped there”*. When she got into bed a few minutes later she got a *“dead feeling”* in all the fingers of her left hand and a cold feeling in the left ear and over part of the left side of her face. Her head felt *“drunk”*. She thought she was having a *“heart attack”* and got very frightened. She woke her husband, who gave her some brandy and the attack passed off. She said the one thing lasted about 10 minutes and that when she got the cold feeling in the left ear she tested her hearing with a clock and found it defective on the left side.

She was not conscious of any respiratory abnormality and her husband did not remark on any *“but then he is so nervous that he would be too upset to notice anything clearly”*. Since that time she had had one or two attacks per month – always when she had just gone to bed and she had had a worrying day. She had to sit up in bed when she got the attacks. Fatigue also precipitated attacks.



The only abnormality discovered on examination was mild diabetes. A hyperventilation test carried on for 8 minutes reproduced all the symptoms including objective diminution of hearing on the affected side. Pulse rate increased from 90 to 120. She said that her heart always beat fast with the attacks.

### **3. Mrs. W. – 22 years. (E.F.)**

This woman complained that for about 3 months she had been getting a *"tight feeling in her chest"* and she felt she had to get outside to get fresh air. Associated with this she would get a stabbing feeling in the left precordium and her heart would beat very fast. On one occasion she developed *"pins and needles"* in her fingers and her hands got stiff. She thought she always breathed fast on these occasions *"but the doctor told me that was just imagination"*. Her hands had been clammy for some time. During the last 2 years, she had lost about 20 lb. in weight but said it was due to her poor appetite. She preferred cold weather but did not find hot weather intolerable. She was admitted to the hospital as a case of thyrotoxicosis and her B.M.R. was found to be raised.

She had been married for 4 years and had three children. *"If I had not been pregnant I would never have married my husband"*. The marriage was very unsatisfactory. He lived apart in a hotel except at weekends and was unfaithful to her.

### **4. Mrs. W. – 29 years. (E.F.)**

Her trouble had lasted 5 years. She had noticed that if she became upset her breathing would become quick and shallow. She would become giddy and would feel a numbness creeping up her arms and round her mouth. The attacks lasted a few minutes.

When she became pregnant two years later the attacks recurred. They never wakened her from sleep but often occurred before she fell asleep. She was particularly prone to get attacks if she was very tired or worried about anything.

She had a lot of financial and domestic trouble and was terrified of having more children.

### **5. G.S. – 37 years. (E.F.)**

This patient complained that for the previous 3 weeks she had experienced periodic attacks of giddiness associated with a *"pins and needles"* sensation in the right hand. She was not conscious of any respiratory difficulty at these times but had always been a prodigious sigher. In addition, she felt tired all the time. She was afraid to climb upstairs in case she got a giddy turn and fell.

She was a widow with three children and had always lived with her mother until a few months before. She felt lonely without her mother and was obviously very dependent. She mentioned spontaneously that it was her mother's absence that was making her ill.

### **6. W.C. – 24 years. (E.M.)**

This patient had had a mastoidectomy and then became worried that his other ear was also affected. He haunted E.N.T. surgeons and was constantly and very transiently reassured. At that time he began to get attacks when in bed about 11 p.m. The first attack consisted of giddiness and a tingling sensation in the left ulnar distribution. He would then get a fishy taste in his mouth and a sharp pain under the sternum which shot up to his shoulder and round his neck. He also got a sharp pain in his left hypochondrium and if he palpated his abdomen would hear a *"lot of gurgling"*. The attacks lasted 10 to 15 minutes and then he would be unable to sleep without a sedative.

**7. B.C. – 54 years. (E.M.)**

This man was a constant visitor to Neurology O. P. D. because of tinnitus in both ears. He had no sign of organic disease apart from arteriosclerosis and as he was worried about being unemployed a job was found for him. However, he reported back the following week to say he could not go to work *"because whenever I have to cross the road I get so dizzy that I fear I will fall and I feel pins and needles in my fingers and toes"*.

**8. E.D. – 48 years (E. F.)**

This woman had been extensively investigated for palpitations. Her story was that suddenly her heart would *"race furiously"*, she would feel slightly nauseous and breathless and her left hand would start tingling. She had been put to bed for months at a time and had had numerous cardiovascular investigations. She was convinced that she had *"a bad heart"*. All investigations were negative and one day during a ward round attention was directed to her because of loud breathing. On examination, her pulse rate was 134/minute and she gasped *"this is one of my attacks"*. She was quite unaware of the fact that she was overbreathing.

**9. M.B. – 29 years. (C.F.)**

Her story was that a year before seeking medical advice her daughter had died suddenly in the night *"from a tuberculous gland burning in her throat"*. For 8 months the patient, who was herself under observation at the TB Clinic because of a past pleural effusion, had been getting nocturnal attacks during which she suddenly became very apprehensive, felt *"a tight feeling in the throat"*, so that she could not breathe properly, but gasped for breath. Associated with this she felt strange and unreal and was so terrified and restless that she would run out into the lonely street at 3 a.m. with her heart racing. The attacks lasted about 30 minutes and afterward she had a feeling of extreme fatigue.

**10. Mrs. B. – 45 years. (E.F.)**

The patient had had several attacks when bad news had been brought to her. One day while sitting on a bus she felt very short of breath and could not think straight. After a few minutes, she had marked tingling in her extremities and felt very dizzy. She felt she just got out of the bus and asked the conductor to let her off. She spoke thickly because her mouth felt stiff and she was markedly ataxic. He thought she was drunk and refused to stop the bus. In desperation, she jumped off and he threatened to charge her.

She also tended to get attacks when she got very hot, e.g. when cooking over a hot stove. She had several burn marks on her arms from occasions when in a confused state from hyperventilation she has swayed against the hot plates.

To complicate matters she had a congenital heart lesion and was convinced that these attacks were a result of her cardiac lesion especially as she had been made respiration conscious by medical interrogation.

**11. Mrs. R. – 38 years. (E.F.)**

This woman complained of constant headaches which were considered to be psychogenic. In addition, she was irritable and sensitive to sound. Sometimes when she had a bad headache she got a feeling as though she was suffocating. Then the fingers of her left hand would begin to tingle. She also said her left arm got "*lame*". She was greatly relieved when this feeling: was reproduced in the left arm by hyperventilation because she was sure it had meant that she was going to get a "*stroke*".

**12. M.S. – 20 years. (E.F.)**

This woman had suffered from dysmenorrhea for several years and from a spastic colon for several months. She said that during the few months before our interview she could get a feeling as though she could not get enough air into her chest. This happened most frequently on retiring for the night. Then she would get a tingling feeling in both hands, especially the left, her legs would feel lame and her mouth so "*thick*" that she could not speak properly. Attacks lasted about 15 minutes, They also occurred during the day when she got nervous and excited and she occasionally "*fainted*" with them.

She had a bad work record – due she said to sickness – and her home atmosphere was not good. She was very resentful about her mother's preference for her young sister.

She was sure she had a bad heart because during the attacks her heart beat so fast and "*several doctors have told me these attacks are due to a weak heart*".

**13. T.W. – 17 years. (E.F.)**

This girl complained that for two years she had been short of breath on exertion and thought there was something the matter with her chest. Four days before she came to the hospital she had to run for her train. On getting into the train she was short of breath. Alarm about her chest resulted in persistent overbreathing for the next 20 minutes while she sat on the train. As the train drew into the station she felt lightheaded and was so peculiar "*that hardly knowing what I was doing I pulled open the door and fell from the moving train*". When she arrived at work she was so shaky and tearful that she was sent home. Two minutes of hyperventilation reproduced the same light-headedness and desire for flight.

**14. W. K.- 17 years. (E.M.)**

This boy said he had been perfectly well until 2 months before our interview. One Saturday night he was sitting on the stoep with a crowd of young people when he suddenly felt dizzy, then became confused and when he came to a few minutes later found his friends holding him down. Six weeks later on a Sunday night under the same circumstances, "*I suddenly felt that I must get more fresh air*."

*My right arm began to tingle and as I got up to walk out I collapsed. I could hear everything that went on around me but could not speak or move. They carried me home and I had three more attacks that night. People always knew when I was going to get an attack because my breathing got so deep."*

He had been converted to the Salvation Army at the age of ten and had played in their band on Wednesday and Sunday nights regularly for 6 years. Just before his attacks began he had decided that he must have more "fun" and had driven up his band playing. However, he felt very guilty about it and both attacks had occurred after taking out a girl.

#### **15. G.H. – 28 years. (E.F.)**

This woman was interesting in that the pattern of her symptoms varied so much. At one time she would feel that she had to sigh a lot and things went black in front of her eyes, or she would feel that something was pressing on her chest, and her throat would close in spasm. At other times attacks would start with a "pins and needles" sensation in her hands and later her legs felt stiff and her hand would go into spasm. The left hand was always more affected than the right and her left shoulder would also draw up. She felt that her stomach was drawn up into a knot and she would get distended with air and belch a lot. Her hands became cold and were wet with sweat.

She had had a bad time with an unfaithful first husband and imagined that her second husband was too interested in a previous girlfriend. Incidentally, she had spent about £200 on her illness and at one time had been thought to be suffering from Jacksonian epilepsy because of the drawing up of the left shoulder.

However, all her symptoms, including the shoulder movement, were reproduced by overbreathing.

#### **16. W. W. – 45 years. (E. F.)**

The patient was quite well until two nights before admission to the hospital. She was sitting reading a book when she suddenly felt faint and began to sweat. She then became unconscious within a few minutes of the onset of her symptoms. She thinks she was completely unconscious for a few minutes. When she came round she noticed that her thumbs were turned into her palms and this happened in spite of herself. Her fingers were blue and she had a sensation of "pins and needles" up both arms. She rubbed her hands together to overcome the abnormal position of her thumbs and remembers that her hands were not weak. She was sweating profusely, her feet were cold and she was breathing rapidly. She could see quite clearly but had no nausea and no palpitations. A friend was present during the attack and told her that her face was blue and her pulse impalpable.

On direct questioning, she remembers that after her evening meal she had a sensation of a lump behind the sternum – like a dull ache which went through to the back and was relieved slightly by breaking wind. Her mother had died of heart trouble a few weeks before this attack. She had had this substernal discomfort on two previous occasions but never so severely.

#### **17. J .K. – 30 years. (Malay woman)**

She complained through an interpreter of attacks for one year. They occurred every 5 or 6 days. An attack usually began about 20 minutes after a meal. It would start with a burning feeling under the sternum. She would begin to breathe heavily and would complain of a pricking feeling in the fingers

and a stiffness of the legs. After about 20 minutes she would lie down, turn blue, and become unconscious. Simultaneously her abdomen would become enormously distended.

A hyperventilation test carried out for 30 minutes reproduced the picture exactly. The distension of the abdomen was dramatic and she broke a lot of wind at this time. A striking thing was that she yawned uncontrollably during the experiment which she apparently also did spontaneously. While semi-comatose with a distended belly she began a curious grunting noise with an action strongly reminiscent of bearing down in labor. She developed a gross lumbar lordosis during the attack.

Apparently, she had one daughter of 12 years and was desperately anxious to have other children.

### **18. M.W. – 32 years. (E.M.)**

This man stated that 5 weeks before our interview he was driving in Johannesburg at 4.45 a.m. He was on his way to pick up a friend with whom he planned to leave on holiday at 5 a.m. He was worried about being on time, and when a robot flashed against him he became agitated. He felt giddy and everything seemed out of perspective. He began to sweat and his heart was beating like a sledgehammer. He had a feeling of submersion "*as though someone was holding my head underwater*". Although he would get air into his chest "*it was an unsatisfactory breath*" and he felt he would die for lack of air. He had a sharp pain over the left breast and a feeling of tension in the muscles of the left forearm.

He immediately thought he had a coronary thrombosis (he had been present at the death of a friend from a coronary thrombosis a few months before) and stopped the car. After a few minutes, he drove on to a telephone booth to which he staggered, but had no change so had to return to the car. He then drove to his friend's flat, holding the door of the car open "*so that he could get enough air*". He drove through several stop-streets and as he parked out the door of his friend's flat a police car stopped behind him and accused him of being drunk. He excused himself on the grounds of illness and entered the flat.

His friend was horrified by his pallor, so phoned for a doctor. The doctor reassured him and arranged for him to have an electrocardiogram done immediately. It's normal. His blood pressure was normal and his pulse rate 100 beats per minute. He was breathing deeply.

Ha was told that it was an "*anxiety attack*" and was advised to go on holiday. The whole attack lasted about half an hour.

He left on holiday the following morning and was away for a month. During this period he had attacks very similar to the first only slightly less severe. Attacks occurred at intervals of 2 or 3 days.

All in all, he had a miserable holiday and was still extremely apprehensive about himself when he returned to Johannesburg. He consulted a doctor who told him he was suffering from the "*hyperventilation syndrome*", explained the mechanism, and told him to hold his breath if he got symptoms. He was enormously relieved at the logical explanation of his symptoms and felt a lot better. That night he woke up at about 1 a.m. with one of his attacks, and on holding his breath the whole thing passed off and he fell asleep much reassured. Three days later he had a mild attack which was immediately relieved by breath-holding.

The night before our interview he was preparing for bed when he became violently giddy and felt he was going mad. He wondered if he were mad to react to stress by overbreathing. He wanted to scream and took a sedative and after about an hour the attack passed off and he fell asleep. He was

not conscious of the old suffocating feeling this time and did not think that breath-holding helped very much.

At the age of 17, he was told when he wanted to take out an insurance policy, that he had nephritis. He was put to bed for a year. Later he was periodically told that he had high blood pressure and albuminuria and got the impression that his days were numbered. He was accepted into the Air Force, however, and served as a pilot throughout the war. He never had any symptoms while flying.

About 11 months ago he began to wake up in the middle of the night with "*pins and needles*" in the left hand and often had nightmares.

He has had a lot of worry about a brother for the last 11 months. He is unmarried. He says he is "obsessional" – e.g. smokes only 8 cigarettes a day and then always at the same time; is very punctilious about keeping appointments; does the same set of exercises every day and must eat at regular times. He has a number of medical friends, some of whom are psychiatrists, and has a strong belief in the power of reason and logic.

After three deep breaths, he was violently giddy and afraid to continue. In less than a minute he had "*pins and needles*" in the left hand and a feeling of tension in the muscles of the left forearm. He then got a sharp precordial pain, a tight feeling around the head, and felt very cold and apprehensive. He said that it was an exact reproduction of his attack.

At his second interview, he demonstrated how practically all day he sucked at his pipe for a few minutes, then took a deep breath as he removed it.

#### **19. G.L. – 52 years. (C. F.)**

This woman complained that for 2 years she had noticed that after even very slight exertion she became short of breath and experienced tightness of the chest, sweated profusely, and had tingling in her toes and fingers and round her mouth. For 3 months she had been awakened at night by a feeling of discomfort in the epigastrium, associated with profuse sweating and "*pins and needles*" in the extremities. Her abdomen became distended and subsided after about 10 minutes then she had broken a lot of wind. The whole attack lasted about 30 minutes and occurred about twice a week.

Hyperventilation reproduced all her symptoms, including the epigastric sensation, which seemed to be due to spasms of the abdominal muscles. She had no evidence of organic disease. Her husband had left her 2 years previously and she was having a struggle supporting her children.

#### **20. E.M. – 52 years. (E.F.)**

This woman had a thyroidectomy 4 years previously. One month after the operation she was recognized as being myxoedematous. During the operation, her recurrent laryngeal nerve had been cut. Eight months after the operation she had her first attack of laryngeal spasm. This was thought to be due to parathyroid removal at the time of the thyroidectomy. The long time interval between the operation and the attack makes this diagnosis improbable. In any case, her serum calcium was normal. She continued to get attacks for years – another unusual feature for the parathyroid type. Her attacks usually occurred at night but occasionally during the day, she felt as though she could not get a deep enough breath and her left hand tingled.

Unfortunately, she was too afraid of the stridor to risk precipitating an attack by overbreathing, but she was undoubtedly a case of hyperventilation.

### **21. P.L. – 19 years. (E.M.)**

This was a second-year medical student who complained of a subjective and objective coldness of the extremities coming on during lectures about 4 times a week and lasting several hours. He had had this symptom for a year and on questioning said that for the same period he had had a feeling of not being able to take a deep enough breath so that he had to breathe through his mouth. During these attacks, he sweated excessively and said he got the sensation *“as if someone was putting dry ice on his toes and fingers”*. He thought he had some peripheral vascular disease. He was going through an unsettling time because he had had a strict religious upbringing and was bewildered by his zoological studies, as they seemed to fit the theory of evolution which his parents said was arrant nonsense. His mother had recently developed peripheral vascular trouble. After the mechanism of his attacks had been explained and demonstrated to him by a hyperventilation test he made an immediate recovery.

### **22. P.L. – 19 years (E.F.)**

Her story extended over 3 months. Her first attack occurred just after her pet dog had been killed. It started with a peculiar feeling in the epigastrium *“as though her stomach had turned to jelly”*. She felt she could not get a deep enough breath, felt giddy and her fingers and toes began to tingle. She sweated profusely. The attack lasted 5 to 10 minutes. Two months later when working under stress she had a series of similar attacks. She always had attacks when she was lying on her bed alone thinking about something miserable. She was a conscientious girl and could not cope with work in an understaffed office.

She was referred to as a case of hypoglycemia.

### **23. Mrs. R.J.- 49 years (E.F.)**

This woman complained that for about two years she had suffered from a tight feeling across the upper sternum associated with a tingling feeling in the left hand and a feeling as though she could not get a deep enough breath. The attacks lasted for about 20 minutes and were not necessarily associated with exertion, emotional stress being often the precipitating factor. On several occasions, she had felt faint. She was not hypertensive or diabetic and hyperventilation reproduced all the symptoms, including the substernal pain.

### **24. R.K. – 18 years (E.F.)**

This girl was referred to the Neurology outpatients department as an epileptic. Her story was that 5 days previously she had just returned from church and saw her mother scolding her sister-in-law for some minor misdemeanor when she *“suddenly dropped to the ground”*. Although unable to speak she could hear everything. Since that time she had had several attacks every day – sometimes a bitter taste in her mouth preceded an attack. She had never bitten her tongue or wet herself during an attack. On one occasion she had had some tingling in her hands-on *“coming to”*.

She was told to overbreathe, which she did recumbent for 4 minutes without developing any striking symptoms. She was then told to sit up and immediately there was a marked increase in rate and depth of breathing and she fell back semi-conscious with her bends in the tetanic posture. Her

mother, watching this, said *“But this is exactly what happens when one gets a fit; she always breathes like that but we did not think it important.”*

The girl had been converted to some religious group and spent all her spare time doing religious work. Her boyfriend, who had been converted with her, had recently deserted both the religious movement and the patient.

#### **25. B.B. – 45 years. (E.M.)**

For about a year he had had repeated episodes of inability to get *“a proper breath”*. He would writhe and struggle at these times, breathing fast and irregularly. About 3 or 4 times a week he would be awakened at night and forced to jump out of bed and contort his body to get some respiratory satisfaction. Sweat poured off him and his abdomen became distended. He felt light-headed.

When his attacks started he had just remarried a woman he had previously divorced. She was extravagant and was making the lives of his children a misery by her scolding and irritability.

#### **26. Mrs. S.T. – 40 years. (E.F.)**

This woman was admitted with a sciatic syndrome. She had no other complaints except that on direct questioning she admitted that periodically in the last 3 years she had had a feeling as though she could not get a deep enough breath. This usually occurred when she was upset about her domestic troubles.

On the third day of admission, she was lying in bed when she suddenly developed this respiratory difficulty. A few minutes later she felt cold and hot by turn and simultaneously a tingling sensation crept up her legs and arms until her face and trunk were involved. Then her hands went into tetanic spasm.

The nursing staff was alarmed and called the houseman. When he arrived she was over-breathing vigorously, had a positive Chvostek and Trousseau sign, and her neck was stiff. He thought it might be a result of the lumbar puncture which he had done that morning but with reassurance, all the patient's symptoms disappeared in about 20 minutes.

The picture was reproduced the following day by overbreathing her for 6 minutes.

On inquiry it was found that her husband was unreliable and unfaithful and she was worried about the care of her children because she had not been visited at all since admission.

#### **27. O.W. – 30 years. (E.F.)**

This woman had had a splenectomy 10 days before she began overbreathing. Her story was that after the operation she felt fine for 5 days. Then she developed watery diarrhea about 3 or 4 times daily. One night she developed a severe paroxysmal cramp-like pain across the epigastrium. The pain waxed and waned but was present throughout the night. She also vomited repeatedly during the night. The following morning during a bout of pain she became very alarmed about herself and noticed that her hands and face were tingling.

A little later the houseman put on a tourniquet to take blood and missed the vein several times. She again began tingling and the obstructed hand went into typical tetanic spasm. At this time although



she herself was unaware of it, it was observed that she was overbreathing. In this case, the patient was peculiarly susceptible to the effects of overbreathing because she was already alkalotic from the vomiting.

**28. W. T. – 19 years. (E.M.)**

This patient developed severe abdominal pain and vomiting which subsequently was found to be due to acute appendicitis. Two days after the onset of the pain he suddenly got "*a peculiar attack*", which consisted of tingling on his face with a "*stiff*" feeling around his mouth; a few minutes later his body became stiff and his hands assumed the tetanic posture. He said the spasm was acutely painful. A doctor was hastily called and relieved the condition by an injection of calcium gluconate.

For the next 2 days, he was free of attacks but still had abdominal pain. On the third day, he was sent to the hospital for an operation. On the day of admission, he had a similar attack although this time his face was spared. He was not aware of any respiratory abnormality though the attack in the hospital was ushered in by obvious overbreathing. Alkalosis due to vomiting made him vulnerable in the first attack and emotional stress due to an impending operation was the factor precipitating the second attack when he was not alkalotic.

**29. G.M. – 17 years. (E.F. )**

This nurse said that for about a year she had tended to laugh and cry very easily. Four months before seeking medical advice she had an attack with the following symptoms: she was laughing a lot then suddenly began to cry. She felt she could not get a deep enough breath and began to pant. After a few minutes, her hands and feet became numb and "*dead*" up to the middle of the forearms. The attack lasted for 50 minutes and was terminated by a doctor giving her a sedative. Three and a half months later she had a similar attack.

On questioning, she admitted that she hated nursing but felt that her parents would be angry if she proposed a change of occupation.

**30. E.P. – 38 years. (E.F.)**

This woman was referred from a country town with a diagnosis of thyrotoxicosis. She said that she periodically got attacks when she had difficulty in breathing, developed "*pins and needles*" in the fingertips, sweated profusely, and got palpitations.

She was going through a period of domestic tension.

**31. F.J. – 39 years. (E.M.)**

For 6 months before admission, the patient had experienced attacks of coldness, pallor, and sweating of the hands. Sometimes the hands felt "*dead*" and he had a tingling feeling in his face. Associated with this he often experienced a feeling of discomfort in the left hypochondrium which extended up to his chest "*as though something was pressing on my heart*". Attacks lasted 10 to 30 minutes and he felt blown up and broke a lot of wind, which relieved the discomfort in the left side. He felt a bit short of breath with the attacks. Attacks usually occurred about midnight waking him from sleep. He had been told that his heart was diseased and had been put to bed for 5 weeks.

One month before his symptoms began his sister-in-law, who was asthmatic, died. Throughout her distressing and dyspnoeic final agonies, the patient was present and says it made a deep impression on him.

**32. C.K. – 26 years. (E.F.)**

This woman had been getting attacks for about 2 months before she came to the hospital.

*She said: "When I get the attacks they start with a feeling as though my nose is blocked, so I breathe through my mouth. I feel smothered and I can't get enough air. I feel as though I am going to faint, so go and lie down. All the blood seems to leave my hands. The saliva dries up in my mouth. I get a 'pins and needles' feeling in my arms as far as the elbows and in both feet. I get a stabbing pain over my heart and break a lot of wind. I water a lot during the attack and my water is very pale. An attack lasts about 20 to 30 minutes".*

She had married her husband when their child was about 2 years old and had been treated unkindly by his family, who did not think she was good enough for him and were constantly interfering in their marriage.

**33. E.M. – 19 years. (C.F.)**

This girl said that she had been well until 10 days before she came to the hospital. Then one night as she lay in bed reading she felt she could not get a deep enough breath. She felt giddy and had "*pins and needles*" in her hands and feet. She had cold shivers and trembled violently. She walked up and down for about 2 hours before the attack finally wore off. Seven days later she had a similar attack at about midnight and was wakened every 1 or 2 hours throughout the night by a recurrence of the symptoms.

She denied all worries but said, weeping, that a favorite aunt of hers had died 3 weeks before.

During 2 minutes of hyperventilation, she got exactly the same symptoms and wept profusely.

**34. H.A. – 44 years. (E.M.)**

This man stated that for 3 months before coming to the hospital he had been getting attacks when he felt anxious. His breathing became stertorous. He felt a "*pins and needles*" sensation in his hands and then his hands "*drew up*" so that he was unable to use them. At the same time he felt faint and unreal "*as though mesmerized*" and on one occasion actually fell over because of the faintness. His speech became thick and he couldn't articulate properly. Attacks lasted about an hour and were relieved by neat brandy.

He had always sighed a lot and for several years had been unable to write while observed because of a violent tremor of the hands and a feeling as though he was suffocating; if he was asked to sign a hotel register he felt incapable of doing so and made some excuse about putting the car away so that his wife could do the signing.

A hyperventilation test resulted in marked giddiness and paresthesia in both hands with a marked tremors of the hands. He refused to continue beyond 2 minutes as he felt so ill.

**35. C.B. – 33 years. (E.M.)**

This man was an immigrant who was *“having a hard and bitter fight”* to make a living in this country. In addition, his wife had severe asthma; *“hearing her struggle for breath at night makes me breathe faster”*. He sometimes had dizzy spells which were so disturbing when driving that he had to park his car and wait until the attack had passed. His main complaint, however, was of a tight feeling across the upper abdomen, *“gripping like a vice”*, which made him feel that he could not breathe properly. When he had this feeling he was extremely restless and if an attack occurred near meal time he was forced to eat standing up.

Experimental hyperventilation reproduced the vice-like feeling *“exactly”*.

**36. P.C. – 36 years. (E.F.)**

This woman was very preoccupied with a pain in her back which had been extensively investigated on many occasions in hospital. She had had a Halsted operation some years before for a suspected mammary carcinoma and was convinced that the pain was due to a secondary deposit. She eventually became a chronic hospital inmate and if discharged would hyperventilate herself into a state of semi-coma and have herself re-admitted as a *“coma of unknown origin”*.

**37. M.B. – 18 years. (E.F.)**

This girl was a nurse who was sitting talking to her friends around the fire one evening when she became aware of a feeling of numbness in her hands and feet. She got up to leave the room and while walking across the room got *“lame”* in her legs and collapsed. She was carried to bed and after a few minutes, her hands and feet assumed the tetanic posture. She was not conscious of overbreathing but said a friend of hers was alarmed when they were sitting in front of the fire *“because her breathing was so deep”*. She continued to have tetanic spasms throughout the night. The next morning she had marked muscle tenderness and a *“feeling of lameness in her legs.”*

She was admitted to the City Hospital as suspected of poliomyelitis.

She denied any worries, but the fact that she was due to go home on leave the next day was thought to be of some significance.

**38. A.M. – 38 years. (E.M.)**

This patient developed left-sided hemiplegia – due to a vascular accident. One month after this he experienced an attack which he described thus: *“I woke up one morning and found my left hand in spasm. I had a tingling feeling on the left side of my mouth. Then my left leg got stiff. My wife had to massage me for about 15 minutes before the spasm passed off. I don’t think I was breathing fast, but my wife says I always breathe too deep”*.

He hyperventilated experimentally for about 30 minutes and then developed well-marked tetany in the left hand which was present for a good 20 minutes before there was any sign of tetany on the other side. Incidentally apart from slight weakness on the left side and positive finger flexion and Hoffman he had very little evidence of hemiplegia. Hyperventilation did not bring out any additional pyramidal signs.

### 39. J.D. – 34 years. (E.M.)

This man was in the hospital with a proven duodenal ulcer. One morning he developed a sharp pain “like a knife” in the left precordium. He asked for the houseman who was busy and was fairly casual about the pain. About 30 minutes later the patient developed tingling in the left ulnar distribution and “broke out in a cold sweat”. His feet and hands then became “dead” and he could not move his limbs or open his eyes. He could hear the medical staff talking around his bed but could not speak. Witnesses say he was breathing heavily at the time though he was quite unaware of this.

### 40. E.F. – 18 years. (C.F.)

This girl came to the hospital complaining of “blackouts” which occurred about 3 times a week, especially when she was in crowds. She never became unconscious but during the attack, she had difficulty in seeing properly and sounds seemed far away. In addition, she breathed fast and her hands were wet with sweat.

## CHAPTER 10 – REFERENCES

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