In favour of the second hypothesis is the fact that the pathological reactions in the valves and myocardium are not those generally accepted as being typical of streptococcal infections. To overcome this difficulty it has been suggested that the patient suffering from rheumatic fever reacts in an abnormal way to streptococcal infection. The joint lesions (which we always found to be sterile) are difficult to explain in terms of an acute infection in view of their fleeting character. If the first hypothesis is correct we would expect that rheumatic valvulitis would develop into malignant endocarditis in the acute or subacute stage of rheumatic fever in a considerable proportion of cases, whereas this result occurs only rarely.

Another argument in favour of the second hypothesis is that other types of streptococci were isolated from heart valves and tissues of cases of rheumatic fever and controls where the blood yielded no such organism. Thus an α streptococcus was isolated from 6 damaged valves and from 2 undamaged valves. A γ streptococcus was isolated from 7 damaged valves. An α streptococcus was isolated from 3 valves of the control series. A pneumococcus, Type IV, was isolated from a damaged valve and an α streptococcus was isolated from the spleen of one of the rheumatic series.

It is obviously dangerous to make dogmatic claims in favour of one type of organism when several have been isolated under identical circumstances. It will be noted, however, that a haemolytic streptococcus was isolated only from damaged valves and never from undamaged valves. Haemolytic streptococci can often be isolated from the blood of cases of scarlet fever if repeated blood cultures are examined, and this slight bacteriaemia probably occurs in ordinary streptococcal tonsillitis, including that which accompanies rheumatic fever. The point at issue is whether or not the isolation of haemolytic streptococci from valves damaged by acute rheumatism represents an actual infection in the valve or a lodgment in the avascular vegetation following a slight bacteriaemia.

The fact that the haemolytic streptococci isolated from throat, blood, valves, myocardium, and brain of any one case were all of the same type (Griffith) would at first appear as strong evidence in support of an actual infection in the rheumatic lesions, but it might be argued that this merely indicates that a blood spread has occurred from the throat. This can be accepted as an argument in favour of either hypothesis, since the results can be interpreted as either a true infection of the tissues or a lodgment of the organism in tissues previously damaged by the rheumatic process.

In conclusion we would say that although at the present time the aetiology of rheumatic fever cannot be said to be solved, we are inclined to support the view that the cardiac lesions are in fact due to infection with haemolytic streptococci.

Summary

Haemolytic streptococci were isolated from the hearts of 5 of 10 patients dying of acute rheumatism and never from controls.

Haemolytic streptococci were isolated from damaged valves, but not from undamaged valves.

Other types of streptococci were isolated from both damaged and undamaged valves, but more often from the former.

The significance of these findings is discussed.

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HYPERVENTILATION AND THE EFFORT SYNDROME

BY

E. GUTTMANN, M.D., L.R.C.P.Ed.*

AND

MAXWELL JONES, M.R.C.P.Ed., D.P.M.

Medical Officer, Emergency Hospital

A syndrome is a number of symptoms frequently observed in combination. "Syndrome" is a descriptive term, and is generally used to avoid premature aetiological conceptions. It may ultimately prove to imply a common aetiology or a common mechanism. More often, however, one finds a limited number of causes liable to produce a syndrome—the typical phrase being, "X syndrome may be due to (*a*), (*b*), or (*c*)." Lewis (1940) applies the term "effort syndrome" to the following group of symptoms: Breathlessness, pain (precordial), exhaustion, giddiness, and fainting; palpitation, headache, and lassitude are additional symptoms of less consequence. This symptom-group "is to be found in a variety of pathological states—for example, in early heart disease, in early phthisis, and in exophthalmic goitre. But it is also found, and in much greater frequency, in soldiers in whom no physical signs of structural changes are discovered."

Among those who show no signs of structural disease a post-infective group stands out clearly; the remainder are classified by Lewis into the constitutionally weak (nervous or physical) and an exhaustive group. The aetiology of effort syndrome is still a puzzle so far as the purely "functional" cases are concerned. Because of the present interest in psychosomatic medicine it is to be expected that the "neurotic" group will attract much attention; and, indeed, no observer with some experience in psychiatric cases will fail to see the similarity between effort syndrome and an anxiety state. This similarity has led to a closer analysis of the symptoms and to an attempt to study effort syndrome by a method which has proved useful in elucidating some manifestations of anxiety—namely, the production of symptoms by voluntary hyperventilation.

Symptoms of Hyperventilation

When a normal person overbreathes sufficiently he will produce two sets of symptoms—(*a*) a tetanic type, and (*b*) some disturbance of consciousness. Tingling in the fingertips (or in the toes or lips), numbness of the extremities, stiffness, and a tendency to characteristic postures (*main d'accoucheur*) up to fully developed tetanic spasms, belong to the former group; the description of the symptoms of the latter group varies not only with their intensity but

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also with the subject's capacity for self-observation and expression. Numbness in the head, dizziness, far-away feeling, faint feeling, sleepy feeling, and fatigue seem to describe the same experience; and "giddiness," often mentioned, apparently does not signify rotatory vertigo but the same impairment of consciousness.

There is a wide variation in the predisposition of normal persons to produce these symptoms: from observation and impression it seems an indication of the person's vegetative lability. Hyperventilation as such an indicator would be of greater value but for the lack of standardization in regard to the amount of air passed through the lungs (or CO_2 exhaled) per time unit compared with normal ventilation. A rough guide to the responsiveness to overbreathing is the threshold for galvanic excitation of peripheral nerves (called Erb's sign in tetany).

Since Grant and Goldman (1920) described spontaneous hyperventilation tetany many writers have confirmed their findings, and the analysis of this clinical picture in both the physiological and the psychological field has made considerable progress. E. Guttmann (1927) described types of patients in whom states of fear or anxiety were accompanied by feelings of oppression or constriction, followed by overbreathing and tetanic manifestations. He assumed that the latent tetanic disposition of the patients and their potential responsiveness to hyperventilation determined the choice and, later, the mechanism of the emotional reactions in question. Kerr, Dalton, and Gliebe (1937) observed the symptoms described in anxiety states with overbreathing. Fraser and Sargant (1938) showed that many hysterical fainting attacks and fits have hyperventilation as a central mechanism. In their observations, as in those described by Guttmann, the attacks were generally precipitated by emotional disturbance, and their patients showed personality and constitutional features suggesting hysteria.

Aetiology of Effort Syndrome

With these experiences in psychoneurotic conditions in mind Soley and Shock (1938) studied the aetiology of effort syndrome. They quote White and Hahn, who found that 80 out of 100 patients suffering from effort syndrome sighed excessively. Soley and Shock contend that in at least one of White and Hahn's cases the patient was hyperventilating. Soley and Shock studied systematically the respiratory disturbances of patients with effort syndrome and the results of the shift in the acid-base equilibrium due to hyperventilation. They state: "Some or all of the symptoms of which these patients complained were reproduced by deep breathing at the rate of 25 to 30 respirations a minute. However, when this respiratory rate was maintained the symptoms were relieved when 2% CO_2 was added to room air." They show in impressive diagrams the changes in the blood chemistry brought about by hyperventilation in effort syndrome cases, and they come to the conclusion that "the respiratory alkalosis resulting from hyperventilation produces the symptoms of effort syndrome." This, of course, is not identical with the causation of effort syndrome, and the authors themselves refer to the fact "that it has been recognized that the combination of anxiety and effort syndrome produces the symptoms listed variously under the diagnosis of 'soldier's heart,' disordered action of the heart, neurocirculatory asthenia, and effort syndrome."

Soley and Shock have shown that in their cases hyperventilation produced alkalosis and the characteristic symptoms together. The questions, however, remain: Is the same mechanism at work in all cases of effort syndrome? Is it able to account for all symptoms of the syndrome? What is the cause of the hyperventilation?

Investigation of 52 Cases

We made an investigation of 52 cases of effort syndrome which had been diagnosed as such in various hospitals and transferred to the Effort Syndrome Unit, where this diagnosis was confirmed. These cases do not include those in which there is demonstrable organic disease, so that for practical purposes they may be divided into three groups—the psychogenic, the post-infective, and the constitutional.

We use the term "effort syndrome" to describe cases which show an excessive physiological response to some forms of exercise or excitement, the most characteristic signs being breathlessness, palpitation, precordial pain, and fatigue. Shortly after their admission, as soon as the routine examination was carried out, these patients were given a hyperventilation test. There is no doubt that hyperventilation produces the alkalotic changes in the blood demonstrated by Soley, Shock, and others, and we therefore felt justified in measuring only the total ventilation as a check of the patient's co-operation. The patient was told to exhale into an anaesthesia mask connected by a corrugated rubber tube with a Siebe Gorman spirometer. The fact that the mask was not fixed by some mechanical device but was held in position by the patient himself certainly led to an experimental error; but as it always pointed in the same direction—the actual ventilation being higher than our figures—we preferred this to the complicated error which in many instances would result from feelings or fear of suffocation when a fixed mask was used. In 34 out of 52 cases the ventilation was measured; in 9 out of the total the ventilation was less than 10 litres a minute. In the remaining cases the reading varied between 10 and 18 litres. The patients were instructed to keep on overbreathing for ten minutes, and 18 did so. Five more breathed over nine minutes. The others gave up after two to eight minutes; they thought the symptoms too disagreeable. Apart from a few cases in which there was a definite exaggeration or hysterical demonstration we were satisfied that the purpose of the test—the reproduction of symptoms—was fulfilled when the patients gave up, or that they had hyperventilated sufficiently to justify the conclusion that they were not abnormally sensitive to overbreathing. Thus the figures in patients with negative results were as shown in Table I:

TABLE I

No. of Case	Duration of Hyperventilation (Minutes)	Ventilation (l per Minute)
24	9	12*
26	10	10
29	10	12
35	10	16
41	10	6
42	10	12
45	9	12
50	10	10

* Considerable loss.

After ten minutes' overbreathing, or when the patient refused to continue owing to tetanic or other symptoms, mostly dryness of throat, he was asked to describe what he felt. He was asked whether he had experienced the same or similar sensations before; after that, what were the symptoms which led to his admission to hospital (that statement was compared with his statements when his routine history was taken); and, finally, he was questioned as to whether he had felt any of these symptoms during or immediately after the hyperventilation. Leading questions were avoided so far as was possible: it was obvious that on the whole the procedure was apt to suggest positive answers as regards reproduction of symptoms by the test.

Findings

The symptoms complained of by the patients as a result of the test are shown in Table II.

TABLE II.—*Symptoms Complained of*

Paraesthesia	24 instances
Giddiness, dizziness, fainting feeling	27 „
Headache	7 „
Tremor	10 „
Pain in chest	6 „
Oppression or shortness of breath	8 „
Marked sweating	5 „

In 6 cases short attacks of deeper disturbance of consciousness were seen. Twelve cases showed marked Chvostek's sign at the end of the test.

In Table III are given the symptoms reproduced by hyperventilation: first, the patient's description at the end of the test; secondly, those complaints in his history which he said were similar to them.

TABLE III.—*Symptoms Reproduced by Hyperventilation (24 Cases)*

Case		
6	Paraesthesia in lips	After vomiting in migrainous attacks
12	„ in fingers	After pain and overbreathing
14	Pain in chest increased	Pains in chest continuously
15	Sinking feeling and fainting feeling	Sinking feeling in attacks
17	Dizzy, fainting feeling	Giddiness, fainting attacks, headache with fainting feeling
18	Dizzy	Dizzy when walking upstairs
20	Weakness all over	Fatigue
21	Headaches	Headaches with choking feeling and difficult breathing
22	Giddiness	Giddiness after exertion
23	Shaky, giddy	Shaky on exertion, giddy
25	Bit shaky	Always inclined to be shaky
27	Weak all over	Fatigue
28	Dizzy, pains in chest, shaky	Dizzy, pain similar to that under exertion, shaky when upset
32	Giddiness, paraesthesia	Same when walking
34	Tight feeling on chest	Sometimes tight feeling
36	Cardiac pain	Spontaneous cardiac pain
37	Head tremor	General shakiness
39	Tight feeling on chest made worse	Constant tight feeling
40	Pins and needles	Same when he walks about
43	Fatigue	Attacks of fatigue
44	Pain in heart, tingling	Cardiac pain, tingling when in forced position
47	Tingling in lips	Felt once or twice before
48	Giddiness, shivering, sweating	Attacks like this
49	Tightness in chest, paraesthesia	Same as after exertion

Although Table III shows that 24 of the cases examined reproduced symptoms after hyperventilation, it would be premature to assume that these were due to biochemical changes brought about by hyperventilation. In interpreting the patients' symptoms and signs it must be remembered that psychological and physiological factors other than the alteration of breathing may influence the result. The test demands some co-operation, some physical effort, and willingness to stand some physical discomfort. The physical effort is accompanied by an increase in the pulse rate; the psychological effect of the test situation may contribute to this acceleration. At any rate, there is good reason to assume that it is not brought about by the increasing washing out of carbon dioxide: the pulse curves reached their peak generally after the first or second minute of hyperventilation, and were settling down again before the first tetanic symptoms were noticeable. In patients No. 20, No. 27, and No. 43, whose main complaint was fatigue, and who after the test had nothing else to complain of, the effect, if any, was surely psychogenic, and in Cases 25 and 37, which responded by tremor only, the mechanism was similarly unspecific.

In the majority of the 19 cases remaining we find that paraesthesia and dizziness (and kindred symptoms as mentioned before) were the symptoms reproduced, and it seems most important to note that only 4 patients complained of more or less characteristic thoracic pain, which, according to our experience, is a symptom met with in 66% of effort syndrome cases. Tightness in or around the chest was complained of in 3 cases (additional to the 4 cases with pain). Palpitations, present in 94% of our cases, did not occur in a single one of the 52 cases as a result of the test, although after the hyperventilation each patient was questioned particularly with regard to this. It must be pointed out, however, that Soley and Shock's patient did experience palpitations after four minutes' overbreathing.

The position, therefore, is roughly that the majority of patients with effort syndrome produce symptoms after hyperventilation, but only half of them reproduce symptoms similar to or identical with those they complain of ordinarily. Among the prominent symptoms reproduced are those of a tetanic kind (paraesthesiae) and disturbances of consciousness often combined with them. In a comparatively small proportion of the cases the cardinal symptoms of effort syndrome are reproduced—namely, "suffocation" and left chest pain. Palpitation did not occur at all. It would appear, therefore, that hyperventilation can be of importance only in a proportion of cases of effort syndrome.

The results would not have been different if the hyperventilation had been carried out more vigorously and for a longer period: the few patients who showed no symptoms overbreathed to an extent far beyond that corresponding to the effort which otherwise produced their symptoms. All the others ventilated sufficiently to reproduce their symptoms or to show tetanic symptoms which were not a reproduction of their clinical complaint. Since the latter patients showed tetanic symptoms for the first time when hyperventilated it is reasonable to assume that their original symptoms are not related to overbreathing.

Discussion

Our findings are well in keeping with some observations which R. V. Christie (1935) made when studying the respiration in the neuroses in general. He came to distinguish "anxiety neurosis"—which may also include many cases of effort syndrome—with an irregular shallow type of respiration, and conversion hysteria where the tendency is to hyperventilate. He says: "The breathlessness [in effort syndrome] is reflected by a tendency to rapid and shallow breathing rather than a true hyperpnoea. In fact, the shallowness of the respiration may in severe cases lead to an anoxaemia and cyanosis."

We can assume as certain that in some of the cases overbreathing is of minor or even of no importance; it is still left to discuss what part hyperventilation plays in those cases in which the symptoms could be reproduced experimentally by this mechanism.

There appear to be two ways in which hyperventilation may operate in producing the syndrome. In the first of these anxiety plus exertion may bring about hyperventilation and subsequently tetanic and kindred symptoms: this is Soley and Shock's view, and it corresponds to our conception of an anxiety state with similar symptoms. This view is best expressed by speaking of "effort syndrome" complicated by hyperventilation syndrome. Some patients describe such a sequence of events, but it is important to remember that hyperventilation fails to produce palpitations, whereas practically all patients complain of them otherwise. This feature of anxiety occurs spontaneously and leads to hyperventilation and subsequently to other manifestations included in effort syndrome. The second possibility is that there is an habitual state of overventilation; it would be of interest to continue Soley and Shock's investigations on these patients in order to determine whether there is a constant alkalotic tendency (alveolar CO_2 and *p*H of blood and urine). The occurrence of such a tetanoid state has been demonstrated in anxiety cases (Guttmann, 1927).

It is obvious that these two possibilities of hyperventilation operating are not mutually exclusive; but it is

certain that only in some cases of effort syndrome is hyperventilation an aetiological factor.

Summary

Fifty-two cases of effort syndrome have been hyperventilated. Only in 50% of them were clinical symptoms reproduced in this way, and in these the symptoms were those which one commonly associates with tetany—e.g., paraesthesiae and disturbances of consciousness—rather than those characteristic of effort syndrome. We feel that in view of our findings we cannot support the contention of some workers that hyperventilation has an important place in the aetiology of effort syndrome.

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OBSERVATIONS ON EFFORT SYNDROME

BY

JOHN D. SPILLANE, M.D., M.R.C.P.

Major, R.A.M.C.

Medical officers in the Forces must now be well acquainted with the characteristic features of effort syndrome. The familiar picture of the distressed young soldier standing before his M.O. apparently short of breath, with an anxious face, rapidly acting heart, complaining of left pectoral distress and dizzy spells, is only too common in our military hospitals. Such patients, both by their number and by their resistance to treatment, constitute quite a problem. During the war of 1914–18 Lewis found that 51% of a group of 558 soldiers with the condition were unfit for all military service. Grant (1925) in a follow-up study of 601 discharged soldiers with effort syndrome reported that 56.2% failed to improve over a period of five years; only 15.3% had completely recovered.

The heart is usually normal, but at first sight the symptoms seem to be those of circulatory distress, and their presence without demonstrable cardiovascular disease is the paradox awaiting explanation. The view currently adopted is that the syndrome arises in those individuals who, whether from hereditary causes or as a result of unaccustomed strain or debilitating illness, have unstable neurocirculatory mechanisms. For this reason Oppenheimer (1918) employed the term "neurocirculatory asthenia" to describe the condition, instead of "soldier's heart," "disordered action of the heart," or "irritable heart of soldiers." This has remained the accepted designation in the United States of America "because it expresses its abnormal character by referring to both neurasthenic state and circulatory symptoms, and at the same time it does not limit the term to 'effort' or 'irritability' or 'soldier'" (White, 1937). Psychiatrists may join issue on the use of the term "neurasthenia" and stress the rarity of that condition in the pure state, but for the general physician the term still denotes a morbid fatigability and irritability of the nervous system. The term "effort syndrome" has probably come to stay, but it is as non-descriptive as it is non-committal.

The following notes are based on observations made at one military hospital in the Home Command during the past year. The cases form a rather ill-defined group, and the borderline is indistinct and easily crossed. At one extreme we find the normal though often bizarre response of the untrained individual to Army life, and at the other the frankly abnormal reaction of the true anxiety case. Effort syndrome cases seem to occupy an intermediate position.

Aetiology

None but the most casual observer could fail to detect the fundamental importance of hereditary and constitutional factors in the development of the illness. The individual is rarely of the "athletic" type; even if his build is average his inclinations are often sedentary. In reality he seems more untrainable than untrained. For some reason or other exertion has always been avoided, and his recreation has usually been fitful and non-energetic. Although in many instances signs of defective physical development are encountered, the existence of similar and even greater handicaps among successful soldiers indicates that some other factor is at work. This is probably a nervous one. Minor physical defects, such as a flat chest, a kyphotic spine, or puny musculature, if accompanied by a robust nervous system do not predispose to breakdown. Neither are they always hereditary; they just as frequently indicate a lack of physical training. The neuropath is less likely to indulge in physical activity than a normal person; he is consequently often incapable of it in later life and may be poorly developed. It appears, therefore, that the fundamental hereditary factors are those which affect the nervous rather than the physical constitution. This is borne out by the fact that there seems to be a higher incidence of minor nervous disorders in the near relatives of such men.

Circulation Time

By the circulation time is meant the time necessary for the blood to pass from one point in the vascular system to another. It is a measure of the velocity of blood flow, which in turn is closely related to the cardiac output and the circulating blood volume. During effort the cardiac output in the normal individual is greatly enhanced and the velocity of blood flow is increased. Even at rest the circulation of the patient with hyperthyroidism closely resembles that of the normal individual during exertion. In both there is tachycardia, increased cardiac output, and acceleration of blood flow. During the last war hyperthyroidism was suspected in many cases of effort syndrome in view of the tachycardia, tremor, flushed skin, hyperidrosis, and warm moist hands which were commonly present. Moderate thyroid enlargement was occasionally observed (Lewis, 1940). But the fundamental difference between these two conditions lay in their response to rest. Patients with effort syndrome improve rapidly, while the accelerated circulation of the hyperthyroid individual remains unchanged.

In 30 soldiers suffering from varying degrees of effort syndrome it was found that the velocity of blood flow, estimated by the saccharin and ether methods, was not appreciably altered. The normal arm-to-tongue circulation time (saccharin method) lies between 9 and 16 seconds (Fishberg, Hitzig, and King, 1934), and in 27 of our patients it fell well within normal limits. In the remaining 3 individuals readings of 8 seconds, 8 seconds, and 6 seconds, respectively, were obtained; these variations were not considered significant. Likewise the arm-to-lung circulation time (ether method) was found to be normal in each case: normal time lies between 4 seconds and 8 seconds (Hitzig, 1935).

These studies were made on patients who had been lying down for fifteen to thirty minutes. They show that under such conditions the velocity of blood flow was