HYPERVENTILATION ATTACKS**A MANIFESTATION IN HYSTERIA**

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It is well known that overbreathing brings about tetany in certain susceptible subjects. Other somatic and psychological effects also result from hyperventilation, but these are apt to escape recognition in clinical practice. At the Maudsley Hospital and out-patient clinics during the last eighteen months over twenty patients were seen who had fits and fainting attacks with hyperventilation as a central feature. Since tetanoid spasms were not always present the part played by overbreathing in the production of the fits had generally been unrecognized.

Mechanism of the Condition

There have been many studies of spontaneous hyperventilation tetany (Goldman, 1922; McCance, 1932; Cumings and Carmichael, 1937; Fraser, 1937; and others). In most cases no pathology has been discovered for the condition, but it has sometimes been found in association with encephalitis lethargica (Barker, 1922; Harrop, 1923) and spontaneous hypoglycaemia (Wilder, 1934). It has also been reported by Goldman (1922) as occurring with pain, nausea, acute infections, and excitement. Changes of mood appear to play a part in certain susceptible individuals. Guttman (1927), discussing the occurrence of tetany in hysterical subjects, thinks that it is a pre-formed mechanism released by overbreathing following or accompanying "Angst," since both of these features are generally seen to precede an attack. Notkin (1930), considering the causation of fits diagnosed as hystero-epilepsy and affect-epilepsy, concludes that one of the mechanisms in the production of the convulsive state is the overbreathing that occurs in these psychopathic individuals under emotional stress and appears to lead up to the fit. It is probable that at least some of his cases are severe manifestations of the type of attack we are about to describe, though we have included none in our series that had true epileptic fits.

Some of our patients' "fits" were typical of those usually described as spontaneous hyperventilation tetany, but many had been diagnosed as fainting or hysterical attacks of varying degrees of severity and did not show tetanic spasms. In all cases, however, hyperventilation occurred throughout the attack, and closer examination revealed other features in common, such as the previous personality and constitution of the patient, and the mode of onset and cessation of the attack. The varying types of attack could also be stopped artificially in the same way. Ample evidence was present for grouping them together and postulating a common mechanism, since the only real difference lay in the severity of the attack, the degree of loss of consciousness, and the varying nature of the motor phenomena met with in individual patients.

The main biochemical change so far demonstrated during the hyperventilation attacks has been a gaseous alkalosis resulting from the overbreathing (Collip and Backus, 1920; Fraser, 1937). The blood calcium alters little, with a slight tendency to rise (Popoviciu *et al.*, 1933; Scott and Cantor, 1933). As yet we are ignorant of the actual mechanisms responsible for the spontaneous onset

of the overbreathing and the increased susceptibility to its effects shown by these patients. These problems are still being investigated.

Practically all our patients were found to have the hysterical personality, so far as this can be clearly defined. They were generally suggestible and emotionally unstable people who easily became apprehensive. They depended on the sympathy and help of others, and showed little persistence in the face of difficulty. Certain constitutional peculiarities were also found in most of them, such as a tendency to brisk reflexes and autonomic irritability. Nearly all were females between the ages of 15 and 30, but one was aged 45. Only two were males.

The attacks were sometimes the sole complaint of the patient, but usually only one of many symptoms in a psychological illness. In a few cases they had been present for many years and occurred regularly with emotional excitement, but generally they were seen only during the acute stage of a depressive or hysterical illness, and disappeared with recovery. The history of the initial attack often revealed that its onset coincided with some particularly severe emotional disturbance. Following the first one, attacks tended to recur whenever the patient's emotions were again aroused. After several fits the susceptibility to them often increased, and some subjects could apparently induce them at will. One man, for instance, had had his first attack in a war hospital, where he had been admitted with the symptoms of bronchitis. A hyperventilation fit occurred one day when he was keeping up the pretence of bronchitis by frequent and exaggerated bouts of coughing. During the last twenty years this mechanism has been so often used by him that it has now become an automatic response to stress of any sort; and though he was able to reduce the frequency of the fits considerably while under treatment he has never entirely got rid of them.

Description of Attacks

Though occurring more readily while under observation of others, they may happen at any time of the day or night. The initial features are very characteristic, and include vague anxiety features such as sinking feelings in the stomach, palpitations, generalized flushings, and trembling. These are followed by a tightness in the chest, by feelings of suffocation and the need for more air, and sometimes by "cardiac" pain. At this stage the patients can generally arrest the attack by not "letting themselves go," but when this stage has passed the attack progresses to its completion unless arrested by an observer. Overbreathing starts when the feeling of suffocation is experienced, and other phenomena then follow in rapid succession. The attacks have three further features after this initial stage which precipitates hyperventilation: (1) interference with consciousness, of differing degree; (2) tingling in the extremities; (3) various types of motor phenomena. In the mildest forms there may be merely some tingling and numbness in the extremities accompanied by mild giddiness. In the severer forms there is a feeling of being "far away," or actual loss of consciousness, and the patients collapse on the floor and lie unresponsive to the usual painful stimuli. In our cases the corneal and light reflexes and control of the sphincters were retained and plantar responses were normal, though the conjunctival reflexes were sometimes lost. The motor phenomena seen are variable: some patients lie limp, but others wave their arms and struggle restlessly; only in some of the more severe cases do periods of tonic opisthotonos occur at the height of the motor restlessness,

and the tongue may then be bitten, and frothing at the mouth sometimes occurs. In the moderately severe cases tetanic spasms may appear in the extremities, but by no means always, and temporary hysterical paralyses are occasionally seen. Throughout the whole of the attack, whatever the severity, rapid and sometimes stertorous respiration continues and eventually subsides spontaneously; the fit then ceases. If left alone the patient remains drowsy and may suffer from headache for some hours afterwards. Sometimes a succession of fits will continue for two to three hours on end, always accompanied throughout by hyperventilation, which increases before each fit. Though attacks subside with a spontaneous reduction of the rate and depth of breathing, they can also be stopped artificially in one of three ways: (1) by closing the patient's nose and mouth and so controlling the rate of respiration; (2) by putting on a rebreather bag; (3) by intravenous injections of calcium chloride, 10 c.cm. of a 5 per cent. solution. Injections of saline given on several occasions to exclude suggestive effects of intravenous therapy were found to be ineffective in stopping a fit.

All these phenomena can generally be reproduced by a short period of voluntary hyperventilation, after which the respiration will suddenly jump into its own tempo and the other accompaniments of the attack follow automatically, as in the spontaneous ones. Though the severity of these induced attacks is rarely as great as with those coming on spontaneously, the two forms are similar in all respects.

Illustrative Cases

The following cases illustrate varying degrees of severity in the type of attack described above.

CASE I

This patient, a girl aged 18, had had hysterical "fits" for the past four months. She was described as being nervous and highly strung as a child, and for many years had been subject to fits of temper and unable to travel much alone. She always had to be taken to and from her work, where her record was unsatisfactory, with frequent illnesses and changes of occupation. The first fit occurred at work, when she collapsed into a semi-conscious state for about an hour; the fits recurred frequently from then on till the time of admission—a succession of attacks sometimes, lasting up to five hours. On admission she had a fit in the waiting-room and again soon after her arrival in the ward. There were further attacks in the presence of new doctors or when she was upset by ward routine. The attacks were described by her as commencing with a feeling of suffocation in the chest and tight feelings in the body; overbreathing then commenced, and the fit would start about sixty seconds later. She lapsed into a semi-conscious state with stertorous respiration, and lay tossing about on the bed without actual tetany of the hands. The fits would continue for an hour or more if she was left undisturbed, but they could always be stopped by an observer—by regulating the respiration or by injecting calcium. Fits of less severity, without loss of consciousness, could be induced by making her overbreathe for two minutes or more. Severe attacks followed the injection of adrenaline, which produced anxiety feelings: tetany would sometimes occur in these adrenaline-induced attacks. The fits gradually became less frequent, following explanation of the mechanism and the immediate stoppage of each fit as soon as it began. The patient was finally discharged—having been free of them for three weeks—to attend the out-patient department, and has not had any symptoms for two months. The ultimate prognosis was not considered good, as the patient had a bad previous personality and denied all overbreathing; it was considered probable that she would use this mechanism again when in difficulties.

CASE II

This patient, an unmarried woman aged 28, was admitted complaining of severe loss of weight and energy, vomiting, paraplegia, headache, irritability, frequent crying, and "fits." A diagnosis of hysteria was made. The history showed that she had always been shy and apprehensive, and the "delicate" spoilt child of the family. At 19 she won a scholarship to an art school, where she spent seven years and led a rather "wild" life, as opposed to her strict religious upbringing. This finally culminated in an entanglement with a married man.

The fits began soon after she went to the art school, occurring in difficult situations. In these she felt a tightness in the chest with a feeling of suffocation, which was followed by overbreathing. Her legs then "gave way" and she collapsed, with tingling, numbness, and tightness in the hands and feet, and giddiness. These attacks became more severe following the affair with the married man. A year before admission she lost control of her legs after a particularly severe fit and developed the other hysterical symptoms shown on admission. It was observed that the fits could be induced after three minutes' overbreathing and stopped by the usual methods. After explanation the patient found that she could prevent threatened attacks by inhibiting the overbreathing. After six months' treatment in the hospital she was discharged to satisfactory and interesting work, and has been free of all symptoms for nine months.

CASE III

A man aged 39 was admitted complaining of "fits" on and off for twenty years, during most of which time he had been in employment. The first fit occurred in a war hospital during a bout of coughing induced to maintain a pretence of bronchitis. Since then they had occurred off and on when he was run down. The fits commenced with cramp in the right abdomen associated with a feeling of suffocation. Overbreathing then followed, and soon resulted in a bursting feeling in the head and numbness in the body, and in fainting. At this stage he was convulsed with violent struggling movements which often took three nurses to control, and he was unresponsive to painful stimuli. Tetanic spasm of the hands and feet was not present. The fits usually lasted half an hour to an hour, but could be readily stopped at any stage by applying a rebreather bag. For three to four hours after a fit he was listless and suffered from a headache. During a short spell of in-patient treatment he was able to reduce the frequency of his fits considerably, but could not completely overcome this long-ingrained emotional reaction.

Diagnosis

Before the attack is actually observed the diagnosis is suggested by obtaining the history of the characteristic premonitory symptoms of tightness in the chest with feelings of suffocation, tingling in the extremities, and giddiness or other forms of disturbed consciousness. Many will deny that they hyperventilate during an attack, but when the overbreathing is actually seen the diagnosis is more obvious, and is finally confirmed by the cessation of the attack when the observer controls the patient's breathing or gives an intravenous injection of calcium. It is also usually possible to reproduce the phenomena by asking the patient to overbreathe voluntarily for several minutes, but some of them do not co-operate readily in this experiment.

True epilepsy can be distinguished by the general features of the fit, especially by the usual absence of the premonitory symptoms described above, the loss of the corneal reflex, the voiding of urine, the frequent occurrence of cyanosis, and the rarity of overbreathing throughout the fit. Hyperventilation fits must also be distinguished from other types of hysterical fit where an

audience is necessary and the manifestations of the attack are mainly an emotional display without overbreathing, which can be stopped by the patient at will.

Treatment

While the emergency treatment of the isolated attack is entirely along physical lines—restriction of the overbreathing by an outsider or the injection of calcium intravenously—nevertheless the prevention of further attacks almost always calls for the psychological adjustment of the patient. Also following an explanation of the mechanism, some patients can be persuaded to arrest the attack in the early stages by a conscious control of respiration. Others, however, deny that they consciously overbreathe or can control their respiration when they become over-anxious. Especially in those who have difficulty in arresting the attacks once the premonitory symptoms of anxiety have occurred, benefit frequently results from investigating the causes of their emotional upset: discussion of their maladjustments and steps taken to alter disturbing factors in their environment often bring about a rapid cessation of the attacks. We failed to persuade a few patients who were deliberately inducing fits to give up this useful refuge from their difficulties.

The giving of calcium, alkalis, or acids by the mouth did not diminish the rapid spontaneous onset of the attack. But the biochemical approach to treatment merits further investigation and offers an interesting subject for future research.

Conclusion

Our study of the above cases has suggested that many hysterical fainting attacks and fits have hyperventilation as a central mechanism. A wide variation is possible in the clinical features of the hyperventilation attacks in different patients, but they appear to fall within one syndrome. The individual variations seem to depend on the severity of the hyperventilation, the degree of autonomic dysfunction, and constitutional tendencies, both metabolic and neurological. Many problems remain as yet unsolved concerning the mechanism of this type of attack, but it is an interesting example of the way physiological abnormalities play a part in the production of apparently hysterical symptoms.

Summary

1. Over twenty cases have been collected in which fainting attacks or fits with hyperventilation were a central feature.
2. The attacks were generally precipitated by emotional disturbance in patients who showed personality and constitutional features suggesting hysteria.
3. The varying features of the attack are described.
4. Diagnosis and treatment are briefly discussed.

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INSULIN-TANNIC ACID-ZINC SUSPENSION IN TREATMENT OF DIABETES MELLITUS

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Much interest has been aroused during the last few years by the introduction into clinical practice of new preparations of insulin, such as protamine insulin ("insulin retard"), protamine insulin (with zinc) suspension, and zinc crystalline insulin. In use these preparations possess the characteristic features of delayed onset in action and prolongation of their maximum effect for several hours beyond that of ordinary insulin, phenomena which have been studied experimentally and clinically by previous workers (Bennett *et al.*, 1937). Suspensions of protamine insulin (with zinc) begin acting in nine to eleven hours, and achieve their maximum effect in fifteen to twenty hours. The value of these new insulins in the treatment of diabetes mellitus is now generally accepted, and has stimulated interest in the clinical potentialities of combinations of insulin with other organic substances and metallic salts. Among the substances studied in this connexion may be mentioned ferrous chloride, magnesium and other allied metals, lipoids, and—of special interest—tannic acid (Bischoff and Maxwell, 1935). The influence of tannic acid on the physiological action of insulin was first demonstrated by Bischoff (1936) during an investigation upon the precipitation of insulin by tannic acid. Insulin in combination with varying proportions of tannic acid, when injected parenterally into rabbits, produced delayed absorption of the insulin with a prolonged hypoglycaemic effect. Gray (1936) consequently gave to diabetic patients hypodermic injections of insulin-tannic acid mixtures (made immediately before use), and noted a delayed but prolonged action of insulin. He also observed that in certain patients erythema and subcutaneous swellings developed at the site of the injections. He did not, however, consider that the skin reactions were a significant drawback to the use of such mixtures. The action of the tannic acid-insulin in animals was further studied in this country by Bavin and Broom (1937), who confirmed the findings of Bischoff and further demonstrated that the properties of the mixtures were enhanced by the addition of zinc (*Lancet*, 1937, **2**, 390).

It is the purpose of this communication to report upon a clinical trial of the Bavin and Broom preparation, with reference to the changes produced in the blood-sugar levels and the local results of subcutaneous injections.

The Effect on Blood-sugar Levels

The blood-sugar levels of nine selected diabetic patients were examined during three periods, in which the patients received exactly the same diet, given at the same times, but with hypodermic injections of different types of insulin. The first test was carried out after injection of ordinary insulin. This was followed by observations after injections of protamine insulin-zinc. Finally the routine was repeated after a dose of insulin-tannic acid-zinc. The latter was a stable light-brown suspension containing the insulin, tannic acid, and zinc already mixed;