in spontaneous tetany resulting from hyperventilation, and to a much less extent in the tetany induced by voluntary overbreathing in normal people, many of the symptoms associated with effort syndrome, etc.—breathlessness, dizziness, faintness, palpitation, tremor—are also present, but tend to be overshadowed by the tetanic spasms. Thirdly, in most cases of spontaneous hyperventilation tetany and in all reported cases of effort syndrome, etc., there is a background of anxiety, emotional stress, or other psychological disturbance.

Conclusions

Two conclusions of importance appear to follow. The first is that the clinical manifestations which may arise from hyperventilation cover a much wider field than is comprised by the term "tetany"; there is much justification for the use of the recently introduced term "hyperventilation syndrome" to include all these manifestations. Of this syndrome tetany is only a component, though the most striking one, particularly when the syndrome appears in normal persons. The second conclusion is that the altered reaction to overbreathing of certain patients as compared with normal individuals is due to the altered psychological state.

This altered reaction might be accounted for in various ways. Thus the changes brought about by overbreathing might fall short of what is required to produce tetanic spasms, so that attention is concentrated on the other components of the syndrome which appear. In the case of effort syndrome which Soley and Shock describe at length voluntary overbreathing caused the appearance of frank tetany immediately following the development of the symptoms originally complained of. A similar result was found in some of Kerr, Dalton, and Glibe's cases. In others, however, tetany failed to appear at all. These might be explained on the assumption that tetanic spasm is inhibited or suppressed while other components develop more or less completely. In more general terms, it may be assumed that there is an alteration of sensitivity of various tissues to the effects of alkalosis, so that, while in normal individuals and in many patients the principal manifestations are shown in the voluntary musculature, in some patients they are shown in the circulatory system, in others in the respiratory system, and so on.

We have not so far had the opportunity of investigating cases showing the hyperventilation syndrome without tetany, and we do not know if these cases produce the same changes in the blood phosphorus and calcium as in those we have reported. Information on this point, however, would be of interest, and, if these changes do occur, of value in diagnosis. Effort syndrome, for example, is, according to Soley and Shock, probably the commonest source of error in the differential diagnosis of organic cardiac disease. Additional help in the diagnosis of this and related conditions would therefore be welcome.

Summary

Five cases of spontaneous hyperventilation tetany, all occurring in young women, are described. In three the tetanic attacks occurred during the course of another illness, while spasmodic attacks were the major complaint in the remaining two.

In blood specimens taken immediately after a tetanic attack the calcium was found to be at a high normal level in four cases and above normal limits in the fifth. In the three cases in which blood calcium was determined in symptom-free periods it was definitely lower than just after the tetanic attack. The inorganic phosphorus of the blood immediately following an attack was in the neighbourhood of 1 mg. in three cases and 2.1 mg. in the other case in which it was determined. In the three cases in which it was determined in symptom-free periods the figures were between 3 and 4 mg.

This great fall in blood phosphorus has not previously been reported in clinical cases, but has been seen in experimental tetany induced by voluntary overbreathing.

The causes of spontaneous hyperventilation tetany have been discussed. Attention has been drawn to the tendency to hyperventilate in persons suffering from anxiety states, and to the tissue alkalosis which results from hyperventilation and which is considered to be the principal factor in bringing on the tetanic attack.

Reference is made to other clinical manifestations associated with hyperventilation, especially effort syndrome and related conditions.

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THE INSULIN TREATMENT OF PULMONARY TUBERCULOSIS

BY

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In the days before there were such things as artificial pneumothoraces and thoracoplasties a great deal of attention was paid to the dietetic treatment of pulmonary tuberculosis. Patients were encouraged to eat heavily at meals and to drink lots of milk in their spare time in the belief that increase in body weight promoted healing. With the advent of surgical procedures dietetic treatment tended to be overlooked or, at any rate, to be pushed into the background. It became the fashion to feed patients on an ordinary full and attractive diet and to regard increase in body weight as an encouraging sign of improvement in local lesions, the credit being given to whatever adjuvant treatment was being employed. Indeed, in one of the latest publications on the subject (Pearson and Day, 1937) the authors had not emerged from this way of thinking, in spite of evidence to the contrary that was accumulating. They advocated an ordinary full diet such as might be given to a boat-race crew in training, although two cases were recorded in which insulin and a high carbohydrate diet had been employed with most promising results. It was the account given by Himsworth (1938) of the gratifying manner in which the diabetic consumptive responded to a high carbohydrate diet together with insulin in excess of his diabetic requirement that encouraged us to try exactly the same regime on consumptives who had not got diabetes. During the past three years we have been feeding an increasing number of our patients on a high carbohydrate diet and rendering their blood sugar low by repeated hyperinsulation. The results suggest the need for a further reshuffling of the cart and horse. Improvement in healing may after all sometimes be the result of regained body weight and not the cause. It certainly appears that improvement can be brought about by forced and "unnatural" feeding.

Technique

The patient receives five injections of insulin, each of 10 to 15 units, during the twenty-four hours. Three of them are given half an hour before the main meals—breakfast, lunch, and dinner—the other two in the middle

of the morning and the middle of the afternoon, and they are accompanied by a fruit drink containing 3 oz. of cane- or grape-sugar. An ordinary standard diet requires very little alteration to turn it into a high-carbohydrate-low-fat diet. At breakfast, porridge or cereals must be taken as well as plenty of toast and marmalade; at lunch and dinner, soups are thickened with flour, puddings with high carbohydrate content are prescribed, and the patient is encouraged to round off these meals with cheese and biscuits—especially the biscuits—to make sure. The patient has a fruit drink always at his bedside to ward off any untimely attack of hypoglycaemia; if ambulant he carries barley-sugar sweets in his pocket. It is interesting to note that without insulin this modification in the diet makes no alteration to the course of the body weight. With insulin the effect is really rather staggering.

As the patient's blood sugar becomes lowered during the half-hour before meals, so he develops an appetite—quite often a craving for food—and a larger meal is eaten than he is accustomed to. But that does not account for the whole phenomenon, because with only three injections a day before meals there is very little effect on the body weight. The part played by the mid-meals injection and the fruit drink is difficult to understand in theory, but in practice it appears necessary for increasing the body weight. Nor does it work so well if the patient has the daily 50 or 60 units split into three pre-prandial injections. In fact, it seems—regrettably—the more injections the better, and in some cases we persuade a patient to have another 10 units, with a fruit drink at bedtime.

The induced hypoglycaemia affects patients in different ways. Some notice nothing amiss throughout the treatment, and one is tempted (sometimes quite successfully) to increase their units, or the time interval between injection and meal, until they do; for both these are elastic and should be adjusted to suit the individual case. The right dosage nicely timed should produce a mild sinking feeling and a readiness—nay, an eagerness—for food. This condition, if the patients are left unfed, develops into what they have christened “the jitters.” They feel tense, their limbs tremble, their heart palpitates, their forehead bursts into a cold sweat, and they become anxious. Very rarely the emotional upset predominates. The patient may feel an urgent desire to howl and to throw things about, and yet realizes the while how idiotic such behaviour is. This condition occurs only at night, and for that reason we rarely give the night-cap dose, which apparently excites it. Two of our patients have developed transient fugue states wherein they have eaten their dinner and conversed with the nurses in a dream state—and have even apparently read their papers. Later they return to consciousness and can remember nothing after a certain moment when the “black-out” began. Both patients did this only at dinner-time, and it was prevented thereafter by reducing the relevant dose of insulin.

The only other untoward effect we have to record is that in some patients the skin becomes sensitized to insulin injections and develops urticaria, first at the site of subsequent injections and later at the site of all previous injections. This is a transient condition, cured as a rule by changing the brand of insulin used. In extreme cases the skin may have to be desensitized by minute doses as in protein desensitization.

Results

Selection of subjects for this form of treatment has always been fortuitous. No regard has been paid to the nature or the extent of their disease or to the presence

or absence of pyrexia. Their only common factor was that on an ordinary diet they persistently lost weight or remained gloomily constant at a weight well below that appropriate for their size. Except for this last circumstance it would seem perfectly fair to compare their average progress with that of the average of all the other sanatorium patients not so treated; but it must be remembered, when such comparison is made, that the average control patients are gaining in body weight on an ordinary diet, and that the subjects were losing, and thus had the dice loaded against them. During the past three years the average increase in body weight of the controls has been $1\frac{1}{2}$ lb. per month (four weeks) per patient. The range of variation is from $\frac{1}{2}$ to 3 lb. per month, due partly to seasonal and climatic influences, but more largely to the variation in the personnel. New patients almost invariably gain weight prodigiously for their first few weeks, so that a month in which many new patients are admitted has an exalted average. On the other hand, a large number of fit ambulant patients on the eve of departure will be reducing their superfluous flesh by increasing exercise and thus lowering the average gain for the time being.

Table I needs very little explanation. It includes every patient who has undergone this special form of treatment.

TABLE I.—Average Cumulative Gain in Body Weight

Case No.	Before Treatment		Zero	During Treatment							
	2 m.	1 m.		1 m.	2 m.	3 m.	4 m.	5 m.	6 m.	7 m.	
	lb.	lb.	st. lb.	lb.	lb.	lb.	lb.	lb.	lb.	lb.	lb.
1031A	—1½	—1½	6 4½	2 10½	11½	15½					
1031B	2	0	7 4½	3 6½	10½						
1031C			7 10½	—½	—½	—½					
1031D			6 10½	7½	10½	13½	14½	18½	20½	22	
1429	4½	1½	8 9	4½	4	6	5½				
1435	6½	3½	7 12½	3½							
1442	1½	1½	5 12½	5½	9½	14	15½				
1447	4	1	9 9½	7	14½	13½					
1478A	0	2½	6 10½	6½	7	14½	21½	25	27½	35½	
1478B	2½	1½	8 8	8½	13½	15½	20				
1478C		2	9 3½	1	—½	1½	4	3½	6	8	
1478D			8 6½	½							
1528	10	4	7 4	6	9	10½	11½	12½			
1535	6½	2	8 1½	3½	8½						
1570A	9½	3½	8 13	4½	7½	12½	16	17½	21½	23½	
1570B			9 3	1½	10½						
1636		1½	8 3	7½							
1638	0	1½	11 5	5½							
1644	1½	½	9 7½	5							
1661		4	10 2½	1½	4½						
1673A	—1	1	7 1½	9½							
1673B		2½	7 7½	3½							
1706	½	—½	8 4	5½	7						
1788			10 7½	16	21½	22½	27	32	38½	46½	
1796		—2½	7 2½	6½	4½						
1835		7	1 ½	5	7½						
1865		—2½	7 2	12½							
Aggregate gain	47½	26½		138½	167½	144½	151½	108½	114½	135	
N o. under treatment ..	14	21		27	20	13	10	6	5	5	
Average for month ..	3.37	1.26		5.14	8.38	11.11	15.15	18.12	22.93	27.0	

Although all these subjects began and ended their course of treatment at different periods during three years (thus largely eliminating seasonal and other influences), the time-datum line has been adjusted so that they appear to be starting their treatment simultaneously.

The weights in the zero column are those recorded immediately before the beginning of treatment; to the left are the monthly differences for the preceding eight weeks, and to the right the monthly differences during treatment. It will be noted that most of the patients were slowly but steadily losing weight before treatment began, and that they at once started to gain weight rapidly. At the foot of each column is the average cumulative gain or loss shown by the patients under treatment at the end of that particular month. Their number diminishes from month to month for various reasons. Only five times has the

treatment lasted more than six months. Where a patient has had more than one course of this treatment his progress on each occasion has been entered separately—for example, Case 1478 A, B, C, and D.

There are one or two points to be noted in this table: first, that in most cases the greatest gain is that recorded at the end of the first month—the record being 16 lb. (No. 1788); secondly, that one or two cases show no gain worth mentioning at all at the end of the first month, but make up for it later on—for example, Nos. 1478 C, 1570 B, and 1031 A. The moral of the latter is: Don't be discouraged if this form of therapy seems to have no immediate effect, but persevere and slightly increase the insulin dosage (as was done in these laggard cases).

These averages I have plotted in graph form (Fig. 1), and to say that they compare very favourably with the curve shown by the average control would be an understatement. The treated patient during the first seven months gains on an average 3.86 lb. per month as against the control's 1.3 lb.—almost three times as much.

FIG. 1

FIG. 2

FIG. 1.—Graph showing increase in weight of the average treated patient compared with that of the average control.

FIG. 2.—Graph showing increase in sedimentin index of the average treated patient compared with that of the average control.

Theory of Symbiotic Equilibrium

The question will be asked, "Are these patients any better off for having gained this prodigious amount of body weight in so short a space of time?" A moment's reflection will show how difficult it is to answer this question at all. The criteria of improvement are, categorically, cessation of pyrexia, diminution and disinfection of sputum, improvement in radiological appearances, improvement in blood stability, and—blessed generalization—improvement in general condition. And here I should like to introduce the term "symbiotic," complete with definition. A "symbiotic" is a patient who is living in a state of armistice with his bacilli. He may have large infected cavities which produce quantities of heavily infected sputum, but for the time being the disease process seems limited to these frontiers; he is apyrexial, ambulant—in fact, he may be employed at a full-time job; his general condition is good and his blood stability is high. He may maintain this symbiotic equilibrium for months or even years. True, the sword of Damocles hangs over his head, but the thread is unfrayed and for the moment his tubercle bacilli are of no more importance to him than his smegma bacilli.

The answer to this question is that insulin therapy will neither heal nor disinfect cavities, but it seems to assist the transformation of a patient with active and progressive disease into a symbiotic. That being achieved, surgical

procedures to obliterate cavities can be undertaken which would have been impossible during the progressive stage of the disease. Some of our most exciting cases are those of patients who, admitted as "dead-beats" and apparently hopeless, have improved sufficiently in their general and local conditions for artificial pneumothorax or even thoracoplasty to be successfully performed.

The Sedimentin Index

By what yardstick can this improvement be measured and compared with the progress of our controls? Both Houghton's index and Medlar's index I find are excellent in their way, but they involve a lifetime of differential blood counts and give in return a very arbitrary figure which is not a measurement of anything in particular. I have a similar objection to the blood sedimentation rate expressed in millimetres fallen by the end of the first hour: it is not a direct measure of anything.

The sedimentin index (Day, 1940), on the other hand, derived from the logarithm of the corpuscles' maximum velocity, gives a definite measurement of those products of tissue destruction present in the blood plasma that cause increased rate of erythrocyte sedimentation—albeit in arbitrary units. For the purposes of this investigation I have chosen in default of any better measurement the monthly sedimentin indices of the subjects and their controls as measurements of improvement or deterioration in their condition.

In Table II I have set out the subjects' sedimentin indices exactly as I have set out their weights in Table I. The

TABLE II.—Average Improvement in Sedimentin Index

Case No.	Before Treatment	Zero	During Treatment				
	1 m.	0	1 m.	2 m.	3 m.	4 m.	5 m.
1031A	0.00	1.96	-0.14	-0.21	-0.14	-0.04	
1031B	+0.02	1.88	-0.03	-0.18	-0.43		
1031C	0.00	1.82	0.00	+0.03	+0.06	-0.07	
1031D	0.00	2.00	-0.23	-0.13	-0.50	-0.58	-0.60
1429	0.00	1.92	0.00	0.00	0.00		
1442	+0.03	1.97	-0.05	-0.07	-0.05		
1447	0.00	1.47	-0.12	+0.03	0.00	-0.19	
1478A	-0.18	2.25	0.00	0.00	+0.02	-0.15	-0.34
1478B	-0.03	2.03	-0.13	-0.03	-0.18	-0.13	
1478C	+0.09	1.76	-0.10	-0.05	-0.10	-0.10	
1570A	+0.05	2.30	-0.10	-0.37	-0.41	-0.48	
1570B	+0.15	2.20	-0.31	-0.38			
1598	+0.17	2.03	-0.03	-0.03	-0.33	-0.48	-0.58
1638	+0.02	2.03	-0.03	-0.10			
1661	+0.13	1.15	-0.15	-0.30	-0.55		
1673	-0.15	2.35	-0.28	-0.35	-0.59	-0.50	-0.59
1706	+0.10	1.92	+0.03	-0.02			
1756	+0.27	2.20	+0.22	+0.15	+0.15	-0.25	
1788	0.00	1.94	-0.44	-0.66	-0.44	-0.82	
Aggregate improvement ..	+0.67		-1.89	-2.67	-3.64	-3.79	-2.11
No. under treatment	19		19	19	16	12	4
Average for month ..	+0.037		-0.099	-0.140	-0.227	-0.316	-0.527

zero column contains their sedimentin index immediately before the treatment started; to the left are given the differences between it and the one noted four weeks earlier, and to the right the gain or loss month by month. The average improvement of the controls throughout the sanatorium is found to be 0.05 unit per month. Before the treatment began subjects were, on an average, deteriorating at the rate of 0.037 unit per month. During treatment the average improvement was 0.105 unit per month.

In Fig. 2 I have plotted these gains month by month against the gain of the average control.

Discussion

The question arises, How long should this treatment continue, and how long does it remain effective? I don't

know. As you see, we start with twenty-seven cases and rapidly drop month by month until at the end of seven months there are only five survivors. Patients tire of being prodded five times a day, and they get positively rebellious when their clothes won't meet in front. I'm afraid my practice is to promise: "This nuisance shall stop when you have gained another 7, 9, 12—or whatever it is—pounds." More often than not I have to keep my word when this is accomplished, and have to be satisfied if they retain that weight subsequently. Of course, those who proceed to lose it—and they never lose it as fast as they gained it—are coaxed to undergo another course. Realizing the possible significance of loss of weight, they are not reluctant.

Incidentally, there was one other respect in which the treated patients differed from the controls: none of them had extra milk. They simply had no time to fit it in.

Summary

The relation between variation in body weight and progress in cases of pulmonary tuberculosis is discussed.

The technique of administering insulin with a high carbohydrate diet is fully described.

Analysis of the results of this regime is found to compare favourably with controls regarding (a) increase of body weight and (b) improvement in the sedimentin index.

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LEAD ENCEPHALOPATHY SIMULATING CEREBRAL TUMOUR

BY

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The present expansion in employment is likely to lead to some increase of industrial hazards to the workers. A case of lead poisoning exemplifying this came recently under our care, and because it simulated closely a cerebral tumour we thought it worth while recording.

Case History

A man aged 41 was for the last two and a half years employed in an arms factory as a range cleaner. His work involved collecting spent bullets from lead dust and sand into which they had been fired during practice. The amount of lead collected varied, but was usually as much as half a ton every night. The atmosphere would become thick with lead dust, and the only precaution against this was a gauze mask which fitted over his mouth on a wire frame. This by no means prevented the lead dust from reaching his mouth, as when he had finished work he would have a thick black layer on his lips and tongue. He used no gloves while working, but always washed his hands carefully before meals, and also made a habit of washing out his mouth. His firm supplied him with one pint of milk daily, which he consumed on the premises. He apparently remained fairly well until July, 1939, when he had a fit and became unconscious for a quarter of an hour. He was subsequently ill and had to stay away from work for a week, the condition being labelled by his panel doctor as one of influenza. It was noticed afterwards that he became irritable and that his memory was failing; he began to have severe frontal headaches and

diplopia on looking to the right. He never experienced abdominal pain, but was troubled with a good deal of cough and expectoration. On September 22 he had another fit, following which he remained somewhat comatose until his admission to Selly Oak Hospital on October 6. The patient has no clear recollection of that period, but remembers that his left arm and leg were twitching and that all this time he had severe headaches and profuse vomiting.

The range cleaners at the factory work in pairs, and we have since heard that the man who helped our patient was taken ill with abdominal pain a week after admission of his workmate.

Condition on Admission.—The patient was very restless and confused, and was vomiting continually. He was emaciated, and had a well-marked blue line on the gum margins. Examination of the nervous system showed the following: palsy of the right external rectus muscle and marked bilateral blurring of the disks. There was slight left facial weakness and disinclination to use the left arm and leg, but these limbs were not actually paralysed. It was difficult to decide whether this was due to some increase of tone on that side or to actual weakness. All deep reflexes were obtained with the exception of the left knee-jerk. Both sets of abdominal reflexes were present and equal, and the plantars were flexor. Astereognosis, wrist-drop, or foot-drop was not detected. Nothing abnormal was found in the heart, lungs, abdomen, and ears. The blood pressure was 120/70; neither blood nor albumin was present in the urine.

PROGRESS AND FINDINGS

Following admission he became even worse, being very restless, mentally confused, and abusive. He had delusions of being robbed and poisoned, and cried without any reason. On October 10 another fit occurred, in which convulsions were generalized, and he was unconscious for a short time. There was no incontinence, and he did not bite his tongue. A lumbar puncture was done on that day, and the C.S.F. pressure was found to be 350 mm. of water. Twelve c.cm. was drawn off, and gave the following analysis: protein, 160 mg. per 100 c.cm.; globulin +; chlorides, 714 mg. per 100 c.cm.; and a definite trace of lead. A blood count on October 9 showed haemoglobin, 70%; R.B.C., 3,660,000; and leucocytes, 11,400. Marked punctate basophilia was present. The twenty-four-hour urine on October 11 contained 1.16 mg. of lead, which is nearly ten times the highest accepted normal level. The blood urea was 60 mg. per 100 c.cm. The Wassermann reaction was negative.

The patient was kept on a milk diet and given sedatives. During the first few days he had three intravenous injections of 10 c.cm. of 10% calcium gluconate. After two weeks there was a decided improvement, and a twenty-four-hour specimen of urine was found to contain only 0.27 mg. of lead. Ten days later the urinary excretion of lead had dropped to the normal figure of 0.12 mg. Ammonium chloride, 15 grammes thrice daily, was then tentatively tried for a fortnight, but no rise in the excretion of lead was obtained, possibly owing to the fact that the dose was not adequate enough to render the urine acid. At no time did he show constipation or complain of abdominal pain. A radiograph of the skull and the long bones revealed no appreciable deviation from normal. The analysis of an extracted tooth yielded eighty-eight parts per million of lead, which, according to available statistics, is within the normal range (Roche Lynch *et al.*, 1934). It is fair to add, however, that the number of teeth so examined is very small.

The patient stayed in hospital for six weeks and made good progress. Towards the end of this time his visual acuity improved so much that he could read small print, and his behaviour, though still somewhat facile, became otherwise quite reasonable. The blurring of the disks had largely subsided, and the other neurological signs disappeared, but the blue line on the gums was still well marked. The C.S.F. pressure returned to normal, and on November 15 the fluid showed 85 mg. of protein per 100 c.cm., with a trace of globulin. The blood urea dropped to 33 mg. per 100 c.cm., and the urea clearance was 74% of normal. We saw him two months after his discharge and found the optic disks and general condition normal.