Again, post-operative vomiting and acidosis are diminished. Three main factors are at present advanced for the causation of these conditions: (1) the psychological factor; (2) disturbance of the pH of the blood; (3) an initial tendency of some patients to ketosis. The preliminary conversation does much to remove any psychic causes, while the constant inhalation of an atmosphere containing sufficient carbon dioxide, yet rich in oxygen, tends to keep the acid-base balance of the blood near normal both during and after operation. This is of great assistance in lessening the third causal factor, especially if the existence of the condition has been recognized before operation and suitable treatment given.

The lungs are more fully expanded both during and immediately after operation, and the incidence of post-operative chest troubles is greatly lessened. Gas pains, too, are not so frequent after anaesthesia by this method. Wilson¹³ has shown that carbon dioxide stimulates peristalsis, and I can bear this out by my own observations. Finally, the patient is the sole indicator of the progress of anaesthesia. The administrator, therefore, must of necessity "keep his eyes in the boat."

CONCLUSIONS

1. The understanding of the phenomena of narcosis with their causation has greatly advanced in the last few years.

2. Anaesthetic apparatus has a very real role in modern surgery, and makes full use of recent knowledge, but by combining several well-tried "tricks" into a simple technique a form of administration has been evolved which embodies the important advantages of mechanized anaesthesia with the ease in use of the open mask method.

3. Induction is simplified and made tolerable. A uniform, well-controlled operating field is assured in any type of case, and operative and post-operative dangers are greatly minimized.

4. The method depends only on facts; the actual technique can therefore be varied infinitely to suit the individual requirements of any anaesthetist.

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A CASE OF COMBINED SCLEROSIS WITHOUT ANAEMIA TREATED BY INTENSIVE IRON THERAPY

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INTRODUCTION

Dr. Sargent's work in investigating and treating a number of cases of combined sclerosis has been largely under my observation, and his treatment of these cases with massive doses of iron, with or without the usual liver therapy, is, in my opinion, a most important advance in neurological therapeutics. The coincidence of subacute combined degeneration of the spinal cord in association with a grave anaemia, pernicious in type, has been known since Lichtheim's publications in 1887 and, more definitely, since the arresting paper in *Brain* by Russell, Batten, and Collier in 1900, but increasing experience shows that the same nervous phenomena occur at times with a normal blood picture. More constant even than anaemia in this disease is complete achlorhydria, as revealed by a fractional test meal, even though digestion and appetite are apparently normal. This evidence of achlorhydria is a valuable point in differential diagnosis from tabes, disseminated sclerosis, and toxic polyneuritis, which are the diseases most likely to be confounded with combined sclerosis, and it is now possible to recognize this condition at an earlier stage than formerly, which is naturally of the utmost importance if cure by therapeutics is available.

Paraesthesiae and tinglings, or "electric" sensations in the hands and feet, with areas of numbness of the extremities, sometimes amounting to severe pains in the

limbs and back, and followed by unsteadiness of gait, are, if accompanied by achlorhydria, diagnostic of subacute combined degeneration, even in the absence of anaemia and spastic phenomena such as ankle-clonus, extensor plantar reflexes, and sphincter weakness.

I have had under treatment by massive iron therapy several cases of subacute combined disease, some exhibiting the full clinical picture of a megalocytic anaemia with ataxic paraplegic symptoms, two others with the paraesthesiae and pains which I have described, associated with ataxia without spasticity and with achlorhydria and pernicious anaemia, and two others in whom the blood picture was normal, although there was marked spastic paralysis and achlorhydria. In all these cases, without exception, the improvement after a few weeks of the treatment was very marked, the pains and numbness disappearing, and the weakness and ataxia steadily improving. The two cases with normal blood pictures were treated with Bland's pill only, 150 grains daily, without any liver therapy. It would appear, therefore, that the nervous degeneration in the spinal cord is in some way dependent upon deficient iron metabolism, which again may be in part associated with achlorhydria. Though the latter would appear to be constant in subacute combined degeneration, its presence does not necessarily set up faulty iron metabolism, since apparent normal health for years may be compatible with complete achlorhydria; some hitherto unrecognized factor must also be concerned in the iron deficiency and the consequent nervous degeneration.

W. H.

It has been suggested in recently published work that faulty iron metabolism is responsible for the nervous degeneration met with in anaemia, both Addisonian and non-Addisonian in type.^{1,2} In the neurological picture obvious improvement was observed after very large doses of iron had been administered in the form of Bland's pill, 150 grains a day. The improvements recorded have now lasted for periods of over a year.

Our observations have led us to concur with the view that the anaemia itself plays no part in the causation.

severity, or onset of the nervous disorder. Indeed, the neurological phenomena seem more closely related to alimentary disturbances producing defective metabolism of iron. Gastro-intestinal dysfunction, as exemplified by achlorhydria, is perhaps the most constant finding in subacute combined degeneration, the accompanying blood picture being very variable both in type and in severity. It is, of course, realized that achlorhydria may be consistent with perfect health, but evidence is gradually accumulating which shows it to be the demonstrable part of an altered metabolism which may lead to an iron deficiency. Castle³ has emphasized the importance of achlorhydria in the causation of pernicious anaemia. He has shown that its development is secondary to the absence of a specific intrinsic factor in gastric juice. It is clear, therefore, that if achlorhydria predisposes to both an iron deficiency and the development of primary anaemia, cases will occur in which these conditions are present simultaneously. A recent article by Heath⁴ has stressed this fact.

The frequency of this dual deficiency accompanying achlorhydria provides, in accordance with our hypothesis, the most satisfactory explanation of the occurrence of subacute combined degeneration following primary anaemia, and helps to explain the failure of liver therapy alone to prevent the onset of nervous disorders in many patients. It is also reasonable to suppose that the nervous system may be affected by an iron deficiency without the development of primary anaemia if, in spite of an achlorhydria, the intrinsic factor is still present in the gastric secretion. Many cases of this type are on record in which the subacute combined degeneration accompanied a hypochromic blood picture.^{5, 6}

If, then, subacute combined degeneration is dependent on alimentary disturbance rather than on the anaemia itself, one would expect to find occasional cases in which an upset in iron metabolism has attacked the cord and spared the haemopoietic system to the degree of slight lowering of the haemoglobin percentage. Such cases do occur, but their importance has been insufficiently recognized, for they provide an argument against the acceptance of the view that subacute combined sclerosis is invariably associated with pernicious anaemia.

Dr. Wilfred Harris was kind enough to draw my attention to a case of this nature under his care, and to allow me to investigate and treat the patient. Special importance was attached to the patient's response to treatment by iron, since the case not only provided a satisfactory test of the truth of our hypothesis but afforded an opportunity for a trial of the efficacy of iron in nervous degeneration in the absence of anaemia. The patient was treated with Bland's pill, 150 grains a day, without other treatment of any kind. It will be seen that a very considerable degree of improvement occurred in the course of two months. The patient had been bed-ridden for some time with severe ataxia and weakness, but has now recovered his power of walking. The case was recently shown at the Clinical Section of the Royal Society of Medicine, but a fuller description and commentary seems desirable in view of the bearing of the case on the problems which we are at present investigating.

CASE REPORT

The patient was a married man, aged 37, whose occupation was that of an hydraulic forgerman. He had experienced good health until two years ago, when he first noticed a feeling of pins-and-needles in his fingers and toes; six months later stiffness developed in the knees and back, and "girdle" pains of the abdomen were noticed. His condition grew rapidly worse, and three months before admission to hospital he had to give up work owing to weakness and unsteadiness of gait, while a definite numbness became evident in his legs

and arms. Other important points in his history were a story of indigestion for the last three years and a loss of appetite, especially for meat.

EXAMINATION AND TREATMENT

On admission there was very marked weakness in both arms and legs, and the patient could not walk without help; gross ataxia accompanied any attempt to walk. Indefinite areas of anaesthesia were found on the forearms, legs, and abdomen. The abdominal reflexes were all absent. Knee-jerks and ankle-jerks were exaggerated, and a bilateral extensor response was present. There was an additional loss of all positional sense in the toes, and vibration sense was much impaired in both legs. A test meal showed complete achlorhydria in all specimens and an excess of mucus in the resting juice, which was of small quantity. The stomach emptied in one and a half hours. The blood count was: red cells, 4,960,000 per c.mm.; white cells, 7,000 per c.mm.; haemoglobin, 88 per cent.; colour index, 0.9; size of cells normal. The cerebro-spinal fluid tests were all normal, and a radiogram of the spine revealed no lesion.

The patient was treated with palliative measures, such as massage, exercises, etc., for five weeks, but in spite of this he became steadily worse. At the end of this period he could hardly raise his legs from the bed; vibration sense was completely lost in the right leg and the ankle-jerks had become absent. Some hesitancy in passing water was apparent, though actual incontinence did not occur.

Bland's pill, 150 grains a day, was now given, massage discontinued, and no other accessory treatment allowed. He first noticed an increase in strength of his legs about three weeks after he began the iron treatment; the tinglings grew less and the girdle pains disappeared. When walking was first attempted it was found impossible to keep him on his feet without the help of two people, because of his gross ataxia and loss of positional sense of the feet. He improved gradually, however, and was later able to use a walking machine. Ten weeks after beginning treatment he was able to travel home to Swindon, and to walk, a little unsteadily, by himself. He has been attending hospital at regular monthly intervals since, and he can now walk well without aid, and can even stand for short periods with his feet together and eyes closed without falling. His ataxia is still noticeable when he is made to turn round very quickly.

The physical signs show the following changes. All abdominal reflexes and ankle-jerks are present; the knee-jerks are not so exaggerated, and areas of anaesthesia are now hard to detect. The vibration sense in the legs has improved, but is not yet normal. The blood picture is: red cells, 5,460,000 per c.mm.; haemoglobin, 95 per cent. A bilateral extensor response is still present. The patient continues to take a daily dose of Bland's pill, 100 grains a day, and has now been under treatment for over six months.

DISCUSSION

This case illustrates well the extent to which spinal nervous degeneration of the combined type may be present without anaemia becoming apparent. That such a recovery should be possible with iron therapy is of interest, since previous treatment in this type of case has been mainly palliative. It seems possible that examples of nervous degeneration of a less degree than was present in this patient may exist, and it would seem advisable to use test meals in the investigation of patients exhibiting such nervous phenomena—whether of a mild or a severe degree—as are usually attributed to anaemia even though no apparent anaemia is present.

A further point deserves consideration. If, indeed, nervous degeneration is associated so closely with alimentary disturbance, then the therapeutic use of iron in large doses may have a more extended field of usefulness. This association occurs in many diseases. One example is pellagra, in which nervous disturbance is often a prominent feature, alimentary symptoms are severe, and hypochlorhydria the rule; although the general symptoms respond to protein diet and vitamin therapy, the nervous

lesions often prove obdurate to treatment. The extent of the usefulness of iron in this disease and in others in which this association is found is therefore being investigated.

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WATER EXCRETION AS A MEASURE OF EQUILIBRIUM WITH ENVIRONMENT

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The use of biochemical formulae as a measure of the emotional tension in psychotic patients has been advocated by McCowan and Quastel,¹ who suggest that the results of blood sugar curves can be used in the formula—

$$\frac{\text{2-hour blood sugar level minus the fasting level}}{\text{The highest blood sugar level minus the fasting level}} \times 100$$

and that the product in manic-depressive psychoses is in numerical proportion to the degree of emotional tension present. The product is known as the hyperglycaemic index. Their results have been supported and correlated by Lockwood^{2,3} in studies of the psycho-galvanic reflex and of the blood cholesterol levels. It is the purpose of this communication to show that the degree of emotional tension or, as it is here called, the measure of equilibrium with environment, can be equally well decided by a water excretion test based on that described by Beaumont and Dodds⁴ as used by Strauss Graunwald. A table showing the relation between the results of water excretion tests and the hyperglycaemic index in fourteen patients is included.

That the renal water excretion is a sensitive index of renal function is well known, but it is so easily affected by nervous influences that its value as an ordinary clinical test is impaired. Addis and Watanabe⁵ have pointed out the variable water excretion from hour to hour and day to day in normal subjects on a constant water intake, while Goodall and Scholberg⁶ have remarked on the low urinary excretion figures shown by many psychotics.

For the water excretion test as used in this investigation the patient is completely starved from 5 p.m. to 4 a.m., when the bladder is emptied. During the next fifteen minutes one pint of water is drunk and the total quantity of urine excreted by 7 a.m. is measured, catheterization being resorted to where necessary. A normal person excretes one pint of urine during this period, perhaps more, but oftener something less. Since renal function is less active by night than by day, it must be noticed that bedtime for patients here considered is 7 p.m., and that the ordinary ward work commences at 5 a.m. Occasionally the test was performed from 9 a.m. to midday after a night's starvation, but no great differences were observed following the change of time. The following results were obtained.

In sixteen patients with melancholia the average water excretion obtained was 5 ounces during the first month after admission, whereas when convalescence had set in the average was 14 ounces. The increase in these patients was slow, and the average time taken to approach normal figures was eight months. In simple uncomplicated de-

pression with retardation the average rise in the excretion figure in six months was from 13 to 21 ounces, while two cases of depression without retardation or agitation, whose only fear after six months was that they might be sent home, gave increased readings from 15 to 17 ounces.

Similarly, early manias averaged excretions of 4 ounces, those ill after two months 6 ounces, those convalescent after this time 12 ounces, and recovered cases 23 ounces.

These figures contrast strikingly with the excretion rates in three placid imbeciles and four simple senile cases. In the former the average excretion in the first week was 13 ounces, and after three months it was 15 ounces, while in the latter a decrease from 15 ounces to 14 ounces was shown in six months. These seven patients were equally at home in any environment if not ill treated.

The following table (Table I) illustrates a series of sugar curves and water excretion tests obtained from fourteen patients.

TABLE I

Case	Day after Admission	Sugar Levels in Mg. %				Water Test	Duration of Illness	Diagnosis	Clinical Measure of Emotional Tension
		Fasting	2-hourly	Highest	H. I.				
1	3rd 4th 15th 19th	— 97 97 —	— 74 79 —	— 123 112 —	— — — —	oz. 10 — 19*	4 weeks	Melancholia agitated	+ — — —
2	4th 8th 15th 30th	— 95 — —	— 180 — —	— 180 — —	— 100 — —	7 — 11 15	4 "	Confusional	++ ++ + —
3	6th 8th 43rd 47th	90 — — 80	115 — — 77	115 — — 130	100 — — —	— 7 15 —	23 "	Mania with some confusion at first	++ ++ — —
4	11th 43rd 49th 95th	— 106 — 110	— 132 — 103	— 153 — 137	— 56 — —	7 — 13 —	Improving after 17 weeks	Melancholia	++ + — —
5	11th 16th 180th 185th	105 — — 98	115 — — 80	144 — — 135	26 — — —	— 10 20 —	Convalescent after 1 year	Melancholia	+ + — —
6	3rd 15th 43rd 45th 53rd	— 93 107 — —	— 143 125 — —	— 154 125 — —	— 80 100 — —	4 — — 6* 4*	Remains acutely agitated	Melancholia	++ ++ ++ ++ ++
7	13th 25th 177th 179th	— 82 94 —	— 118 78 —	— 132 125 —	— 72 — —	10 — 28 —	30 weeks	Mania, recurrent	+ + — —
8	2nd 15th	— 72	— 88	— 134	— 26	15 —	14 "	Melancholia	— —
9	41st 45th 56th 59th	— 80 — 88	— 100 — 90	— 105 — 118	— 80 — 7	2 — 13 —	16 "	Mania with confusion at first	++ ++ — —
10	3rd 7th 20th	— 78 —	— 113 —	— 130 —	— 34 —	4 — 13	11 "	Melancholia agitated	++ + —
11	100th 115th 116th	— 107 —	— 81 —	— 150 —	— — —	8 — 12*	17 "	Melancholia	++ + —
12	5th 16th 28th	— 99 —	— 148 —	— 165 —	— 74 —	5 — 7	8 "	Mania with delirium at first	++ ++ ++
13	2nd 57th 130th 135th	— 80 — 85	— 128 — 78	— 145 — 128	— 74 — —	4 — 18 —	23 "	Melancholia agitated	++ ++ — —
14	5th 15th 27th	— 81 —	— 139 —	— 162 —	— 71 —	4 — 12	9 "	Mania with confusion at first	++ ++ +

H. I. = Hyperglycaemic index of McCowan and Quastel.

* These results were obtained between 9 a.m. and midday.

† = Rough measure of emotional tension as observed clinically, where ++ = well marked, + = present, and — = absent.

There is a fairly general agreement between the two tests. Case 1 in this table illustrates the value of these estimations. This patient made two attempts at suicide