diathermy. But if the patient is stout-hearted there is no reason why a little more should not be diathermized.

Subsequent to the operation, as the effect of the anaesthetic wears off, the patient will feel a little soreness, which will continue for a few days. But, particularly if the surgeon is careful to avoid the pillars of the fauces, little or no complaint is made, and the patient is able to submit to the treatment from start to finish without being away from work for a single day.

The first séance is succeeded by others at intervals of about a week or ten days, each time one or two or more areas of about 1 cm. in diameter being coagulated. The length of the course depends, naturally, upon the size of the tonsils and the amount the surgeon feels called upon to coagulate each time. I find the duration of my treatment to be from two to four months. Towards the end of the time there will remain to be disposed of a few isolated mounds or clumps of lymphoid tissue in the recesses of the tonsil bed, and adhering to its capsule and to the faucial pillars. When this stage is reached infiltration anaesthesia may be required, and the needle electrode is then handy for getting at these less accessible remnants.

In general, we avoid too extensive a coagulation at any one séance, chiefly because of the risk of bleeding during separation of a large, deep slough. In view of the possibility of this accident the patient should remain within reasonable reach of the operator throughout, so long as there are any sloughs to come away. Personally, I have not yet seen serious haemorrhage in these cases, but I know that it does occur, and, indeed, circumstances being as they are, an occasional haemorrhage is to be looked for. But there can be no doubt that the risk is minimized if the surgeon contents himself with modest advances and restrains his own and his patient's desire to bring the treatment to an end as early as possible.

By the foregoing method, carried out with care, patience, and perseverance, one can destroy all the tonsil tissue in the pharynx without seriously taxing the patient's fortitude, and with a minimum of scarring.

One interesting observation has been made, and that is, that patients quite frequently report improvement in their remote symptoms—rheumatic pains and so on—immediately after the first applications of the diathermy. The explanation probably is that the diathermy sterilizes the tonsil of bacteria beyond the area coagulated and so cuts off the supply of toxins.

There can be no doubt, in my opinion, that diathermy coagulation will come to be the method of choice for removing tonsils in adults. It is much superior to London paste and the galvano-cautery, and it may even challenge comparison with the ordinary surgical operation, particularly in delicate and nervous adults. It is, of course, unsuitable for children.

ADDISON'S ANAEMIA:

THE OCCASIONAL FAILURE OF LIVER THERAPY.

BY

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It has lately become almost a platitude that a case of anaemia which does not respond to treatment by means of a liver diet should not be diagnosed as Addison's anaemia. It is therefore of interest to consider the following three cases, on clinical grounds diagnosed as Addison's anaemia, which failed to respond to liver therapy. With these cases were simultaneously treated others of the same disease which gave a response to liver in every way comparable with that described by Minot and Murphy. Moreover, the methods of diagnosis and treatment employed in both the successful and unsuccessful cases were identical.

CASE I.

The patient, a single woman aged 58, was admitted on March 20th, 1928, with a twelve months' history of sensory changes with loss of power in the hands and legs. She had a sister suffering from anaemia, and the only important fact about her previous

medical history was that she had been operated on for gall-stones in 1925.

Physical Signs.—The tongue was clean and glazed, but not sore; there was subjective and objective evidence of involvement of the nervous system; achlorhydria was present; the Wassermann reaction was negative. The van den Bergh test gave an indirect positive reaction of 2 units. The blood count was as follows: red blood corpuscles 3,460,000 per c.mm., haemoglobin 77 per cent., colour index 1.26, white blood cells 4,000 per c.mm. Megalocytosis and anisocytosis were present.

Treatment.—On the above evidence a diagnosis was made of subacute combined degeneration of the cord, accompanied by a moderate degree of Addison's anaemia, and treatment with 8 oz. of liver a day and dilute hydrochloric acid was instituted.

Progress.—The treatment was continued for over six weeks, but the blood picture remained unchanged and there was no improvement in the nervous symptoms. The patient was discharged on May 5th, 1928, and stopped taking liver and hydrochloric acid. On December 18th her blood was examined again, and we were astonished to find that the anaemia had spontaneously disappeared and she now had a normal blood count. There was no concurrent amelioration in the nervous symptoms. Further observation on this case was not possible, but an inquiry made in March, 1929, elicited the information that the patient was alive and in much the same condition as when we saw her in 1928.

Commentary.

Clinically this case was one of Addison's anaemia with subacute combined degeneration of the cord, though confirmation of this diagnosis could be obtained only by post-mortem examination. The occurrence of a spontaneous remission afforded proof that the bone marrow was capable of responding to a suitable stimulus, but the conclusion appears inevitable that the liver could not provide such a stimulus in this case.

CASE II.

A man, aged 51, by occupation a miner, was admitted on October 5th, 1928, complaining of progressive weakness for twelve months. The patient had one brother suffering from some variety of anaemia, but otherwise his family history and personal medical history afforded no significant data.

Physical Signs.—The patient showed evidence of intense weakness and wasting; he was drowsy and febrile. There was no evidence, subjective or objective, of involvement of the nervous system; achlorhydria was present; the Wassermann reaction was negative; and the van den Bergh test gave an indirect positive reaction of 5 units. The blood count was as follows: red blood corpuscles 1,150,000 per c.mm., haemoglobin 25 per cent., colour index 1.2, white blood cells 2,400 per c.mm. The urine had a specific gravity of 1022, and contained a trace of albumin. Megalocytosis and anisocytosis were present.

Treatment.—The patient was given 8 oz. of liver each day, with liver extract to supplement the deficiency when he was unable to take the full dose. Dilute hydrochloric acid was given as well.

Progress.—The patient went steadily downhill, became comatose, and died on October 24th. On October 15th the blood count had dropped to 1,000,000 red blood corpuscles per c.mm., with haemoglobin 23 per cent. From this date onwards the quantity of liver extract was doubled, and arsenic in the form of sulphostab was administered as supplementary treatment.

Post-mortem Examination.—The liver, kidneys, and spleen gave a marked iron reaction; the haemolymph glands were prominent, and the bone marrow showed the megaloblastic reaction typical of Addison's anaemia. There was no evidence of any complicating disease.

Commentary.

This is a case in which the diagnosis of Addison's anaemia was confirmed by post-mortem examination, and the only reason that can be advanced to account for the apparent failure of liver therapy is that the anaemia was a severe one. It may be suggested that the bone marrow was so overwhelmed with toxins that it had become too far damaged to respond; on the other hand, many patients with low blood counts are known to respond well to liver therapy.

CASE III.

This patient, a man aged 45, by occupation a collier, was admitted on October 24th, 1928, complaining of progressive weakness for ten months, loss of weight and sore tongue, and gastro-intestinal disturbances.

Physical Signs.—The patient was weak and showed signs of wasting; his tongue was clean and glazed, his spleen palpable, and evidence was obtained, both subjective and objective, of involvement of the nervous system. The Wassermann reaction was negative; the van den Bergh test gave a positive indirect reaction of 5 units. The blood count was as follows: red blood

corpuscles 1,100,000 per c.mm., haemoglobin 23 per cent., colour index 1.1, white blood cells 2,400 per c.mm. Megaloblasts and megalocytes were present, and there was also anisocytosis.

Treatment.—This was the same as that given in Case ii.

Progress.—The patient continued to become weaker, and on December 5th, despite a blood transfusion performed early the same day, he died.

Post-mortem Examination.—The liver, kidneys, and spleen gave a marked iron reaction, and the bone marrow showed a megaloblastic reaction. No other disease was present, except anthracosis of the lungs.

The remarks applied to Case ii by way of comment also apply to this last case.

These three cases afford some evidence against the prevalent view that every true case of Addison's anaemia must necessarily be benefited by liver therapy. So far, very few unfavourable results following this treatment have been published, but two of Fraser's series failed to respond for no accountable reason. G. Guiani of Genoa found that 15 per cent. of his cases gave no response to liver, but possibly many of the patients were moribund when they came under treatment, and their bone marrow was thus unable to respond. If the existence of a small proportion of unsuccessful reactions to liver therapy is established it must materially alter the prognosis of Addison's anaemia; above all, it imposes the necessity of withholding the promise of a hopeful outlook until the effect of liver administration has been observed for a sufficient period.

It has not been suggested that liver destroys the exciting cause of the anaemia. As, moreover, it is known that agents as essentially different as malaria and benzol can give rise to an Addisonian anaemia, it is probable that there are many different exciting causes, and it can hardly be expected that liver should prevail against every one of them. It seems reasonable, then, to assume that in some cases the exciting cause is so powerful that it overcomes any benefit that might be expected to accrue from the administration of liver.

In conclusion I wish to thank Dr. A. F. S. Sladden, pathologist to the Swansea General Hospital, who examined the blood in each case and conducted the post-mortem examinations, and Dr. Daniel E. Evans, senior physician to the Swansea General Hospital, who allowed me to investigate and report on the cases.

THE ACETIC ANHYDRIDE TEST IN CEREBRO-SPINAL FLUID.

BY

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THIS test was described in 1923 by Boltz, who found positive results in all cases of general paralysis and certain other types of neuro-syphilis. During the next few years various authors concluded that the reaction was of diagnostic value in these conditions. The test is performed as follows: to 1 c.cm. of the cerebro-spinal fluid 0.3 c.cm. of acetic anhydride is added, and the mixture is shaken; 0.8 c.cm. of sulphuric acid is added very gradually, drop by drop. A positive result consists in the development of a colour which has been described as "blue-pink," "lilac," or "purple."

The test is similar to the glyoxylic reaction of Hopkins and Cole, which was discovered as a result of their investigation of a test for protein described by Adamkiewicz. This consisted in the development of a violet colour when protein was treated with glacial acetic acid and concentrated sulphuric acid. Hopkins and Cole showed that the reaction was dependent on the presence of glyoxylic acid as an impurity in the acetic acid. The constituent of proteins responsible for the reaction with glyoxylic acid is tryptophane.

In 1927 the similarity between the "Boltz test" and the glyoxylic reaction was pointed out by Duncan, by Blix and Backlin, and by Walker and Sleeper. These authors brought forward evidence that the acetic anhydride test was identical with the glyoxylic reaction, and that the positive results in cerebro-spinal fluid were due to protein.

Positive results were obtained when the acetic anhydride test was applied to tryptophane solutions, or to egg-albumen solutions of concentrations of 0.03 per cent. and over. As would be expected from these facts, it was found that many non-syphilitic cerebro-spinal fluids yielded positive results.

The appearance recently in the *British Medical Journal* of a paper by Piotrowski prompts me to draw attention to these findings, and to record some personal observations which confirm the view that the acetic anhydride test is a protein reaction similar to the glyoxylic reaction.

Several samples of acetic anhydride were examined, and all gave a positive reaction with protein. The less pure samples gave the more intense reactions, but the purest samples obtainable gave positive results. The colour produced showed the same absorption spectrum as the colour produced in the glyoxylic reaction.

A series of twenty-four cerebro-spinal fluids from various cases was tested; these included cases of epilepsy, cerebral tumours, general paralysis, disseminated sclerosis, hysteria, and various types of meningitis.* The intensity of the colour given in the "Boltz test" was roughly proportional to the total protein content of the fluid, and the colour given by fluids from cases of general paralysis was indistinguishable from that given by fluids of the same protein content derived from non-syphilitic patients. For example, the fluid from a case of general paralysis (total protein 0.18 per cent.) and the fluid from a case of meningitis (total protein 0.15 per cent.) gave colours exactly similar in tint and intensity. On another occasion the fluid from the same case of general paralysis had a lower protein content (0.05 per cent.), and then gave a negative result with the "Boltz test."

It appears impossible to fix a limiting concentration of protein below which the reaction is negative. Apart from the variations in the samples of acetic anhydride used, there are variations in the conditions of the test as ordinarily employed. The heat developed during the addition of the sulphuric acid is an important factor, and different results can be obtained with the same protein solution by varying the rate at which the sulphuric acid is added. If the mixture is carefully cooled after the addition of each drop of sulphuric acid, so that the temperature of the mixture is not allowed to rise above room temperature, no colour develops, even in fluids which give a definitely positive reaction when treated in the ordinary way. This applies to the fluids from cases of general paralysis as well as non-syphilitic cases. If the mixture, which has been kept cool during the addition of sulphuric acid, is subsequently heated the typical colour develops.

Owing to the crude method by which the test is usually performed, a definite limit of protein concentration below which reactions are negative cannot be fixed accurately, but, in my experience, with pure samples of acetic anhydride it is approximately 0.03 to 0.05 per cent.

It is therefore probable that the "Boltz test" is a protein reaction similar to, or identical with, the glyoxylic reaction. It may be due to some substance (? glyoxylic acid) present as an impurity in the acetic anhydride, or derived from the acetic anhydride in the course of the test. If acetic anhydride is completely hydrolysed by heating with an excess of water for an hour under a reflux condenser, the product still gives the violet colour with protein on addition of sulphuric acid.

If the view here taken is correct, it seems surprising that the test should ever have been regarded as diagnostic of syphilis of the central nervous system. As far as the earlier papers on the subject are concerned, the explanation seems to be the lack of fluids of high protein content among the non-syphilitic controls. In the investigations of Boltz, Grossman, and Harris all the fluids came from patients with mental disease. No figures for the protein content of the fluids are given, but in any such series it would be expected that the syphilitic fluids would have the highest protein content.

Among those who regard the test as diagnostic of general paralysis or neuro-syphilis, Greenfield and Carmichael seem to be the only authors who have studied non-syphilitic cases

* For the majority of these fluids I am indebted to Dr. E. A. Carmichael.