labour from no evident cause (a case probably of eclampsia without convulsions), finds similar conditions in the pituitary as Bell. In the pars anterior he also finds "large cells whose protoplasm stains feebly with any stain—exhausted secretory cells (?). The pars nervosa has been invaded by the large eosinophil cells from the anterior lobe."

Brain.—*Post-mortem* findings in the brain in eclampsia are "moderate oedema of the convolutions, sometimes with anaemia, sometimes with congestion." These changes may reasonably be brought about, as explained before, by sudden spasm and contractions of the blood vessels of the brain.

Liver.—"The most typical changes *post mortem* are albuminoid degeneration, with haemorrhagic and anaemic necrosis. These focal necroses occur near the small portal vessels." These changes are produced by spasm of vessels as explained above. Hepatic degeneration with marked necrosis of liver cells has been produced in animals experimentally by Carro by continuous injections of infundibulin. This spasmodic necrosis is probably the causative factor also of the condition of acute yellow atrophy of the liver in pregnancy.

Kidney.—"The most common changes in the kidney in a majority of cases are those of an acute nephritis, and this is hard to distinguish from an acute parenchymatous nephritis." The cause of these changes in the cells of the kidney I explained above.

I think I have adduced sufficient evidence to show that eclampsia—in common with all the other so-called toxæmias of pregnancy—is brought about not by some accidental external agent, nor is it the result of some morbid derangement producing poisons or toxins from either the foetus, uterus, or intestine, as most of the theories advanced on the toxæmias of pregnancy assume; but that it is essentially a physiological process *overdone*—due to an excess, rather than a perversion, of an essential product.

Why nature should, in the process of gestation, so often overshoot her mark, and thus defeat her own aim, is due to the comparatively short evolutionary experience she has had of this, her newest experiment in reproduction—the placental form.

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CONTINUOUS TREATMENT IN SURGICAL TUBERCULOSIS.*

BY

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IN recent years so much work has been done with regard to the treatment of tuberculosis of the bones and joints, and in both medical and lay papers so much has been written, that further insistence on principles now firmly established and fully recognized may seem unnecessary. The work of Sir Robert Jones, of Sir Henry Gauvain at Alton, and of Calvé, Calot, and others at Berck-sur-Mer and elsewhere, and the discussion at the Annual Meeting of the British Medical Association in 1921, have shown clearly what can be effected by organized and continuous treatment in this direction. But it is doubtful whether in this part of the country we have followed in the footsteps of our leaders as closely as we might. Perhaps on close examination it may be found that although we have acknowledged our belief in continuity of treatment in surgical tuberculosis, this belief has never been translated into action, and, as we are told, "Faith without works is dead." Those of us who are surgically minded are still too apt to regard an operation as the whole treatment in this disease, instead of a mere incident, and an incident which continuous treatment has made less frequent and of diminishing importance. Others, who, having been impressed by

certain unsatisfactory results following operation, have decided to do without it, have made no serious or continued attempt to establish the conditions necessary to avoid operation. These mistakes appear to have arisen because we do not continually bear in mind that surgical tuberculosis is a disease whose duration is measured in years and not in months, and that during the whole of the active period and for some time after we cannot afford to relax our vigilance for a moment. If we do, we run the risk of lengthening the necessarily long duration of the disease, and of permitting the existence and increasing the severity of deformity. Relaxation of continuous supervision in the early stages leads often to rapid spread of the disease, to abscesses which might have been prevented, to deformity difficult or impossible to correct when the condition becomes obsolete, and to the necessity for serious and often mutilating operations. Those who advocate early operation in these cases insist on careful and continued after-treatment. How much more, then, is it necessary if the condition is too advanced for complete eradication of the tuberculous lesion? When such an operation is apparently successful, how unpleasantly often does the return of disease, or at the very least deformity, show that after-treatment has been too brief! How seldom, in spite of all that has been written, does recovery take place without leaving the patient a cripple!

The necessarily long course of the disease makes continuous in-patient treatment in general hospitals almost impossible, and leads almost inevitably to periods of neglect of, or loss of interest in, treatment. During such intermissions the disease breaks out afresh into activity or deformity increases. Once it is recognized that deformity can be prevented, and when present can be minimized only while disease is active, the present disconnected methods will have to give way to a continuous supervision.

In Bradford there are no fewer than six institutions which deal with surgical tuberculosis. Of these, three act entirely independently of the rest. They are hospitals whose constitution precludes long periods of in-patient treatment. The other three are, in theory, linked, but since no one of them was primarily established to deal with surgical tuberculosis, they suffer from the defects of overlapping and lack of co-ordinated surgical supervision. They are a sanatorium to which, along with phthisis, cases of active surgical tuberculosis can be sent; a cripple school where, amongst other conditions, surgical tuberculosis believed to be obsolete can have the benefits of such treatment as is possible for a finally fixed deformity; and a special hospital where, with other orthopaedic cases from this school, the large percentage of cases of supposed obsolete tubercle which prove to be active can have emergency treatment. The last two institutions contain the germ of an ideal scheme and afford at the present time the only attempt to solve the problem of continuous treatment of surgical tuberculosis in the city.

To get the best results it should be possible for all children suffering from this condition to obtain systematic treatment during the whole period of active disease and for some time afterwards. If we include the infants' and children's clinics and exclude the special hospital fed from the Cripple School we have seven separate "nets," the gaps between which are filled by the medical practitioners of the city. The active cases thus "caught" in many instances escape from the net before they are "cured" (if I may venture to continue the metaphor) and are picked up again if seriously crippled at the medical inspection of school children. They may thence be sent to the Cripple School, but too late to prevent or cure deformity. Hence the weak point in Bradford is the provision for active or acute cases.

The Cripple School has accommodation for about two hundred children, of whom some 40 per cent. are or have been cases of surgical tuberculosis. The cases of active disease can and do have the benefit of recumbent, postural, and other forms of active treatment—extensions, plaster, and ultimately of properly made and fitted celluloid jackets and other appliances. By a wise provision such cases are resident from Monday to Friday in each week, and for the week-end or during periods when active surgical interference is required are transferred by ambulance to the special hospital linked to the school. In suitable cases they spend their week-ends at home. Under these favourable conditions I have been able to keep cases of spinal caries recumbent for two years and to watch them through the critical period of their gradual return to active life. And all this has been possible without interruption of their education. An extension of this scheme to include admittedly active cases is all that is needed to put

* A paper read before the Bradford Medico-Chirurgical Society on January 10th, 1922.

the treatment of surgical tuberculosis in Bradford on a proper footing. The school is healthily situated, sanatorium conditions exist, and facilities for nursing and massage are adequate. It is not too far from the town to justify a possible complaint of the parents that they are losing sight of, or touch with, their children.

In an industrial town such as Bradford, where the cases are sufficiently numerous, the most effective way of dealing with the problem is also likely to be the cheapest. It is primarily a hospital problem applied to children of school age; but since such cases under proper supervision are not ill, school teaching with suitable manual training can, and should, be given at the same time. There is no reason why in-patient (recumbent) and out-patient (ambulatory) cases should not be taught at the same institution, and this would have the further advantage that medical supervision by the same people would be practicable for both classes of case, and the after-treatment of the cured would be in the hands of those responsible for the cure. Much overlapping would be prevented, much better results would be obtained, much needless deformity would be saved, education and treatment would continue without gaps, and a larger percentage of useful citizens would be the ultimate outcome. An after-care association for those beyond school age would round off and complete the scheme.

THE NITROGEN METHOD AS AN AID TO DIFFERENTIAL DIAGNOSIS IN MENTAL DISEASE.

BY

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In certain types of mental disease, and notably in general paralysis of the insane, clear evidence is to be found *post mortem* of degeneration of the brain tissues, whilst in other forms of mental disorder exhaustive macroscopic and microscopic examination has failed to reveal anything abnormal.

Since a correct diagnosis is essential to correct treatment and to prognosis, and since general paralysis is incurable in the present state of our knowledge, it is obviously a matter of considerable importance to establish any diagnosis of that disease with as much certainty as possible, and as early as possible, more especially because there are other forms of mental disorder which may simulate it very closely in the earlier stages.

Apart from my nitrogen method, which is the subject of this paper, there are essentially two laboratory methods which have been extensively employed to clinch or to negative the diagnosis arrived at by clinical observations. These are the Wassermann reaction (in the blood and in the cerebro-spinal fluid) and the reactions for excess of protein in the cerebro-spinal fluid. In both these ways valuable information may sometimes be obtained, but their limitations are considerable. A very thorough discussion of the subject will be found in Goodall's Croonian lectures.¹ Here it need only be mentioned that the applicability of the Wassermann reaction as a diagnostic test for general paralysis rests on the basis that general paralysis is a syphilitic manifestation. It will be seen, however, from the discussion of the matter above cited that different observers have found widely differing percentages of positive results in undoubted cases of general paralysis—a fact due, no doubt, to the inherent uncertainty of the reaction, for it is well known that experienced observers frequently fail to obtain similar results from the same sample. Generally speaking, it appears that positive results, whether in the cerebro-spinal fluid or in the serum, are obtainable only in something like 60 or 70 per cent. of undoubted cases of general paralysis. This compares unfavourably with the 90 per cent. of positive results in cases of syphilis, and it should also be pointed out that positive results were found in 7 per cent. of the cases other than general paralysis.

The reactions for protein in the cerebro-spinal fluid are numerous, but all aim at revealing the presence of an excess of protein in the fluid, the presence of such protein being indicative of abnormal degeneration of the brain tissue. The rapid and simple Nonne-Apelt reaction, in which any proteins are salted out by the addition of an excess of ammonium sulphate, has been the most used and is probably the most reliable procedure. Unfortunately, this test frequently fails

to give a positive result in cases where the products of degeneration are not present in the form of coagulable proteins. In fact, it would hardly be too much to say that the Nonne-Apelt reaction cannot be relied upon excepting in cases where degeneration is so definite and well marked as to make any laboratory assistance superfluous to a physician of experience.

These references to the Wassermann and protein reactions are designed to show that the diagnosis of general paralysis is by no means so simple and straightforward as it is sometimes represented to be, and that there is every justification for the laboratory to provide additional methods such as that referred to in this paper to assist the clinician.²

Choline.

Many workers have endeavoured to detect in the cerebro-spinal fluid during life evidence of the breakdown of cerebral tissue, which undoubtedly occurs in general paralysis, brain softening, and some other conditions. Many years ago it was claimed by some that in such degenerative conditions choline (derived from the phosphatides of the brain) could be found in the cerebro-spinal fluid. Others, repeating this work, failed to confirm the results. In an investigation of this question I was fortunate enough to discover not only the truth of the matter, but also an explanation of these contradictions. There is no choline in cerebro-spinal fluid, and there is no ammonia. But when cerebro-spinal fluids, especially if they are derived from cases of general paralysis, or obtained *post mortem*, are treated in the (chemically speaking) barbarous way adopted by some of the investigators, decompositions occur, and there are produced (1) a substance which, although not choline, gives some of the alkaloid reactions shown by choline, and (2) ammonium salts which form a platinichloride only distinguishable from choline platinichloride by the polarization method first suggested and employed by Kauffmann.³ If a freshly obtained fluid is worked up with due precaution, neither the pseudo-alkaloid nor the ammonium platinichloride is obtained.

THE NITROGEN METHOD.

It has been mentioned that the object of the choline researches was to obtain evidence during life of abnormal degenerative processes in the brain. The finding of choline or ammonia in the cerebro-spinal fluid would have been such evidence, but when the investigation just described had shown that these substances were not really there, it still seemed probable that evidence of the presence of products of degeneration might be obtained by other means. The origin, use, and fate of the cerebro-spinal fluid are still obscure, but as it is in intimate contact with the tissues of the central nervous system, it is natural to suppose that its composition might reflect any changes in the katabolism of those tissues.

In these circumstances I devised a method for the rapid and accurate estimation of the total nitrogen present per cubic centimetre of the cerebro-spinal fluid, and in 1913⁴ published an account of the method and of the results obtained by means of it in about seventy cases of mental disease. It is unnecessary to describe the method in detail, the more so as the paper is available in English.⁵ It need only be mentioned that 1 c.cm. of cerebro-spinal fluid is heated with fuming sulphuric acid, the reaction mixture is diluted with water, made alkaline, and distilled into a series of Nessler cylinders, where the ammonia is estimated by Nesslerization, as in water analysis. The whole process, excepting perhaps the actual Nesslerization, can be carried out by any laboratory boy of reasonable intelligence. The process is also fool-proof. In view of the very small quantity of material, certain precautions have to be taken in regard to cleanliness, and in this matter a little supervision may be required, but the effects of any carelessness are at once apparent.

Differential Diagnosis by the Nitrogen Method.

Since 1913 the nitrogen method has been in routine use in this hospital as an aid in diagnosis. The claims made for it at that time have now been substantiated over a much larger number of cases, and it is the object of this communication to describe the results which have been arrived at. These results are set out graphically in the accompanying Diagrams 1 and 2, which include 254 cases.

A word is necessary in explanation of the graphic mode of representation employed in Diagram 1, which is due to my wife, Mrs. Helen L. Stanford, B.Sc. Lond. In the original paper it was shown that the nitrogen number (NN) being the