peripheral nerves. At any rate, it was not a case of ascending myelitis leading to rapid and extensive softening of the cord. This is shown by the preservation of faradic excitability, of the functions of the bladder and rectum, and absence of tendency to bedsores, or of anaesthesia. A certain mystery has always hung over Landry's paralysis because it has so frequently happened that no morbid changes in the nervous system have been discovered after death. The disease was capable of abolishing function and of destroying life, without leaving behind any lesion or demonstrable alteration of tissue to indicate in what manner those results had been brought about. There are doubtless cases in which the nerves and spinal cord have been examined by modern methods and no pathological changes have been found. In rapidly fatal cases the action of the poison on the nervous tissues may be sufficient to cause death before characteristic changes of structure have had time to develop. On the other hand, many of the earlier cases occurred before it was customary to examine the peripheral nerves, so it is probable lesions in some cases have been overlooked. When inflammation involves all the elements of a mixed nerve it is usual to find that both motion and sensation are affected. In the case before us we may regard the lesion as principally affecting the whole system of lower motor neurons. The axis cylinders of the motor nerves are outgrowths of the ganglion cells of the spinal cord, medulla, and pons. The chief stress of the destructive process would be found in some cases in the peripheral nerves, and doubtless most often there because of their distance from the centre, and in others in the ganglion cells themselves. And here we can see an explanation why motor power has been recovered in some parts of the body and not in others. So long as the nerve cells themselves are not destroyed, there is possibility of regeneration of axis cylinders and of recovery of muscular tone and motor power, while if the cells themselves undergo degeneration there is permanent muscular atrophy and motor paralysis. This has occurred notably in the cell groups innervating the extensors of the forearm and toes and the small hand muscles. Although the morbid process has exercised a selective action on the motor fibres of mixed nerves, it is probable there has also been interstitial neuritis, which by pressure would cause irritation of sensory fibres. In this manner the tenderness and pain in many of the muscles can be accounted for. Neither hyperaesthesia or anaesthesia of the skin occurred, which appears to show that nerves containing sensory fibres only were only slightly affected, if at all.

Dr. Michell Clarke, in an interesting article in the *BRITISH MEDICAL JOURNAL* for September 12th, 1908, would limit the term "Landry's paralysis" to cases in which the lesion is confined to the anterior cornual cells, degenerative changes being nowadays demonstrated by Nissl's method, but which would have been passed over by earlier pathologists, thus giving rise to the notion that Landry's paralysis caused no morbid changes of tissue. This proposition apparently assumes that true Landry's paralysis is always fatal, for the morbid anatomy of a patient who recovers must always be more or less a matter of speculation. In the clinical sense I think the case I have related is sufficiently near the type of Landry's paralysis to be included under that name. Dr. Clarke goes on to describe a case of ascending paralysis due to toxic polyneuritis. There was great muscular wasting, the reaction of degeneration was present, and the patient died after an illness of about three months. At the *post-mortem* examination the peripheral nerves showed a very advanced degree of neuritis. But this was not all, for many anterior horn cells, especially in the cervical and lumbar enlargements, showed degenerative changes, such as disappearance of the Nissl bodies, vacuolation, and disappearance of the nucleus.

The physical and chemical properties of the poison causing acute ascending paralysis probably vary, and its nature in different cases is but little known. In one published case⁴ micrococci have been found in the ganglion cells of the cord. Whatever the nature of the poison, it probably circulates in the blood like alcohol and the diphtheritic poison, and exercises a selective action on the lower motor neurons, the peripheral portion of which frequently suffers most. Another example of the selective action of a poison is that of the late effect of the syphilitic poison on the sensory protoneurons or on the pyramidal

cells of the cortex cerebri, producing the diseases known as tabes dorsalis and general paralysis respectively. The notion that Landry's paralysis is associated with no morbid tissue changes of permanent character can no longer be maintained, or that no muscular wasting occurs in cases that recover. This question was fully inquired into by the late Dr. Ross, and he "clearly showed that many cases have been reported which in the early stages were clinically indistinguishable from cases of rapidly fatal ascending paralysis, in which, when convalescence was protracted, some of the muscles became atrophied, and gave partial or complete reactions of degeneration to electrical tests,"⁵ *main en griffe*, and double ankle-drop being not uncommon distortions.

REFERENCES.

¹ For an account of a rapidly fatal case see *BRITISH MEDICAL JOURNAL*, February 27th, 1909. ² *Allbutt's System*, first edition, vol. vi, p. 701. ³ *Allbutt*, op. cit., p. 697-8. ⁴ *Allbutt*, op. cit., p. 702. ⁵ *Allbutt*, op. cit., p. 700.

ON THE USE OF CERTAIN NEW CHEMICAL TESTS IN THE DIAGNOSIS OF GENERAL PARALYSIS AND TABES.

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THE diagnosis of general paralysis of the insane is for two reasons a more important matter than the diagnosis of most forms of insanity. On the one hand, thanks to the clinical observations of Pilcz, Kraepelin, and a host of other workers, with the pathological researches of Nissl and Alzheimer, we have a clearer picture and more exact knowledge of the course and nature of the disease than about almost any other psychosis, so that we can foretell what events are likely to occur in it, and take measures to guard against them. On the other hand, the prognosis is more fatal and the lethal termination more rapidly reached than in any other form of insanity, so that it is important to recognize the condition as soon as possible, and to get the patient's affairs arranged on the basis of that knowledge. Although in a pronounced case the clinical picture is one of the sharpest in the whole of medicine, yet in an early or non-typical case the difficulties in diagnosis are often exceedingly great. So much is this the case, that it is found in asylum practice that the majority of the patients are admitted either with an erroneous diagnosis, or else comparatively late in the course of the disease. Hence the additions to our knowledge that of late years have accrued from a study of the cerebro-spinal fluid in the disease have been welcome and valuable aids to the practitioner. These newer laboratory methods of course can never replace accurate observation of the well-known physical signs of the condition, any more than Vidal's test has replaced the employment of physical examination in the case of typhoid fever, but a knowledge of them is of the utmost importance when we have to deal with obscure and doubtful cases.

Before detailing some personal researches it will be well to review very briefly present knowledge concerning the cerebro-spinal fluid in general paralysis, and this is best done, perhaps, by mentioning the various points in the chronological order of their discovery.

The first step in this connexion, and still one of the most important, was the discovery, made in 1900 by Ravault, Vidal, and Sicard, that lymphocytosis in the cerebro-spinal fluid is one of the most constant accompaniments of both general paralysis and tabes. Many forms of cells are found, the most significant being large mononuclear lymphocytes and plasma cells. When in a non-febrile malady the lymphocytosis is very pronounced, then it may be regarded as practically pathognomonic of general paralysis. The cell increase is greater at the onset of the disease—a fact that obviously enhances its value in diagnosis.

A year later the discovery was made by Achard, Loefer, and Lanby that considerable quantities of proteid are to be found in the cerebro-spinal fluid in general paralysis and, to a less extent, in tabes. As the present paper is chiefly concerned with this question, consideration of it may be conveniently postponed for the moment, and it will suffice here to mention the well-established facts that in normal cerebro-spinal fluid the quantity of proteid is minimal, that in the diseases in question the increase is mainly an increase in globulin, and that this increase is not always parallel with the degree of lymphocytosis, tending on the whole to develop later than this phenomenon.

The next discovery was the startling one made by Wassermann in 1906, that the cerebro-spinal fluid in general paralysis contained substances which, when combined with the syphilitic virus, have the power of inhibiting haemolysis. It will be remembered that in 1900 Bordet demonstrated that in various processes, of which haemolysis may be taken as a type, three bodies are essential components. These are, first, the antigen, or substance that is being destroyed—bacterium, blood cell, etc., as the case may be; secondly, a non-specific substance, or complement, found in all blood serums; and, thirdly, a specific substance, or amoceptor, found only in the serum of an individual that has been previously injected with the corresponding antigen—the amoceptor being thus evoked as a response to the foreign body. It follows that if two of these three bodies are present in a fluid and cytotoxicity does not take place, it must be due to the absence of the third; thus, if the antigen is not dissolved on being added to its corresponding amoceptor, the complement must be missing. In this way we can test for the presence or absence of complement. Now Wassermann found that syphilitic virus obtained from a fetal liver in which spirochaetes had been demonstrated, when in the presence of the cerebro-spinal fluid of a paralytic, made a combination with it and the complement present in any blood serum. This complement was thus taken up or fixed, and was no longer free to cause haemolysis when added to red blood cells and haemolysin in the way just mentioned. For this test he first incubates for an hour the syphilitic liver emulsion with the suspected cerebro-spinal fluid and the complement-containing serum of a guinea-pig; he then adds the mixture to an emulsion of washed red blood corpuscles of a sheep and some serum of a rabbit that has been several times injected with sheep's blood. If the blood cells dissolve—that is, if haemolysis or laking takes place—then the complement must have been free to do it, and could not have been fixed by the preliminary incubation. Wassermann maintains that this is due to the absence of any syphilitic antibody or amoceptor in the cerebro-spinal fluid. On the other hand, if laking does not take place, then the complement must have been previously fixed by the combination of the syphilitic antigen from the liver and syphilitic antibody in the cerebro-spinal fluid.

While Wassermann's observations have received the widest confirmation, his interpretation of the phenomenon has met with serious criticism, and is to-day practically discredited. It is quite true that the reaction just described is positive in over 95 per cent. of cases of parasyphilis, and negative in other diseases, so that beyond doubt there is some substance in the cerebro-spinal fluid which when combined with syphilitic virus has the power of fixing complement and thus inhibiting haemolysis. But the nature of this substance is a far more disputable matter. That it is not a specific syphilitic antibody seems to be certain from the observations made, first by Weil and Braun, that it shows the same power of inhibiting haemolysis when combined with other substances than syphilitic virus—for instance, lecithin. It is now known that the place of the syphilitic antigen can be taken by a number of substances, including lecithin, bile salts, brain emulsion, normal liver emulsion, etc.; and Benecke has recently brought evidence to show that the efficacy of the syphilitic liver in Wassermann's experiments is due to the presence in large quantities of a peculiar soap pellicle that surrounds the fat droplets characteristic of that lesion.*

Leaving, however, the theoretic aspect of the question, we have to note that all workers at the subject—notably Plaut, Morgenroth and Stertz, Marie, Levaditi, Yamanouchi, Weil, Eichelberg, and Neubauer—are unanimous as to the high practical value of Wassermann's discovery. It may be said at once that it is the most certain sign of general paralysis we at present possess. Its only disadvantage is the complexity of its application, and before it can be of much value in practice it will have to be considerably simplified.

Two other methods may be briefly mentioned. In 1907 Fornet and Schereschewsky stated that the serum of a luetic patient gives a specific precipitate with the serum of a paralytic. This observation has been received with much scepticism, and Plaut, who is perhaps the most reliable authority on the subject, says that this precipitate is just as common with normal serum. In 1908, Porges and Meier showed that the cerebro-spinal fluid of paralytics causes a heavy precipitate when added to the lecithin emulsion. This is of interest when one remembers the important part played by lecithin in the Wassermann reaction.

The theoretic interest that the increase in globulin has resides in the fact that most authorities agree in attributing to it the origin of the substance active in the Wassermann reaction. The trend of opinion is towards regarding this as resembling choline and nucleo-proteid in being katabolic products produced in the course of the disease. The relation between globulin and the substance that gives the Wassermann reaction becomes therefore a matter of great interest, and the phenomenon of globulin increase receives an accession of both practical and theoretical importance from these considerations.

Now, the experience of the past eight years has amply confirmed the fact of globulin increase in general paralysis and its very great value in diagnosis, and the object of the present communication is to consider two new methods for the precise observation of this increase, together with the results of our experience with these methods. The first of them was described some five months ago by Noguchi of New York; the second has not hitherto been described.

There are, of course, several methods in general use for the separation of globulin from albumen, but all of these leave much to be desired in reliability and delicacy. For the cerebro-spinal fluid the following are those that have been most employed. Guillain recommends that the fluid be saturated with magnesium sulphate and then heated; a precipitate indicates the presence of globulin. Nissl, Henkel, Nonne, and Apelt, who have all published extensive monographs on this subject, add to the fluid an equal quantity of a saturated ammonium sulphate solution. Cimbald adds a saturated zinc sulphate solution. In our experience, however, these methods sometimes fail even after twelve hours to give a precipitate with fluids that at once give one in the two tests next to be described.

We shall consider first the technique of these tests and then the results obtained.

Whichever test be applied, it is essential first of all to be sure that no blood or pus has contaminated the fluid to be examined; results are of little value, even in cases in which there was a very high lymphocyte count, on account of the secondarily derived globulin. The test may be carried out at any date after the puncture, provided only that the fluid be clear.

The Noguchi reaction consists in the addition of 0.5 c.cm. solution of 10 per cent. butyric acid in normal sodium chloride solution to 0.1 c.cm. of the fluid to be examined, the application of heat, subsequent addition of 0.1 c.cm. of 4 per cent. sodium hydrate solution, with a further application of heat. The test tube should be read within three hours. A distinct opalescence is frequently found to occur even with the normal, but in cases of general paralysis and tabes a characteristic precipitate of a peculiar flocculent character forms. The flocculi tend gradually to fall, so that after twenty-four hours at the latest the bottom of the tube is occupied with a fairly bulky precipitate, whilst the supernatant fluid is clear. In performing this test care must be taken to ensure the absolute purity of the butyric acid. This was evidenced during the experiments by the following occurrence. We had finished the brand of butyric acid obtained from Dr. Makins, of New York,

* This subject was fully discussed by Dr. Mott in the second of the course of lectures on Syphilis of the Nervous System, published in the JOURNAL of February 20th.—ED. B. M. J.

that had been found to be satisfactory, and on December 7th tried a new brand in 6 cases. To our surprise all of these gave negative results, a finding that was shown, by comparison with some that Dr. Noguchi kindly placed at our disposal, to be due to impure butyric acid.

The second test referred to is as follows: 2 c.cm. of a saturated solution of ammonium sulphate are placed in a test tube, and 1 c.cm. of the cerebro-spinal fluid is gently run on to the surface in the way done in the Heller nitric test for albumen. The formation of a ring at the junction of the two liquids constitutes a positive reaction. The ring is clear-cut, thin, greyish-white, and has the thickness of a thin piece of paper. It should form within three minutes, and within half an hour it may be observed that the surface of the ring shows a delicate mesh appearance resembling a fine cobweb. Indirect illumination must be used, or it may escape detection. For this purpose we have constructed a black-lined box into which the test tube can be inserted and viewed at right angles to an electric bulb which is fixed within the box a few inches away. In applying the test it is essential to see, first, that the ammonium sulphate is pure, so that the solution is neutral and not acid; and, secondly, that the solution is quite saturated, which is best ensured by the use of heat in its manufacture.

We come now to the question of results. Up to the present we have examined only 27 cases, but the paucity of our material is partly compensated for by the uniformity of our findings, which has encouraged us to believe that the tests in question will prove to be of considerable utility.

The Noguchi test was applied in 15 syphilitic cases and 12 non-syphilitic. It was negative in all of the latter except in 1 case of tuberculous meningitis. Among the negative cases were 5 of dementia praecox and 4 of tumor cerebri, conditions which are frequently very difficult to distinguish from general paralysis. Among the 15 syphilitic cases were 12 untreated and 3 treated cases. None of the latter gave a positive reaction, while all of the former did so. The 12 positive cases comprised 3 of tabes, 5 of general paralysis, 1 of tertiary syphilis, and 3 of syphilis of the nervous system. The test was thus positive without exception in all cases of syphilis or parasyphilis that had not had recent treatment, and negative in all other cases examined.

The effect of treatment was shown not only by the non-reaction of the cases under treatment, but also in the disappearance of the reaction seventeen days after initiating treatment in a case that had previously shown a marked positive reaction. It is known that there is an excess of proteid in the cerebro-spinal fluid in no chronic disease of the nervous system apart from syphilis, and that agrees with our findings. In cases of acute infection, on the other hand, there is often an excess of proteid present, whatever be the nature of the infection. This was so, for instance, in the only case of this kind—one of tuberculous meningitis—that we have been able to examine.

The ammonium sulphate ring test was applied in all of the above cases except two of tabes. The results agreed absolutely with those obtained by the Noguchi test, being positive whenever this was positive and negative whenever this was negative, so that the list of cases need not be repeated. The amount of proteid present in normal cerebro-spinal fluid is insufficient to give a ring with ammonium sulphate, though it commonly gives one with pure nitric acid. In general paralysis the amount is increased tenfold, and far exceeds that reached in any other disease, except of course acute meningitis. In the differentiation of general paralysis from syphilis with no nervous manifestation, we would rely not on the mere excess of proteid in the former, for that occurs in both conditions, but upon the striking extent of the excess. This can be roughly estimated with the ammonium sulphate ring test in three ways—by noting first the density of the ring, secondly the time that elapses before its appearance, and thirdly by the dilution with which it appears. The last point has greatly interested us, particularly, however, in connexion with the globulins of the blood serum in syphilis, a matter with which we are not here concerned. Our observations on the point are as yet incomplete, but it would seem that we have in the dilution test a means of readily estimating the amount of globulin present, and therefore the degree of certainty of the

diagnosis. We have several times, for instance, obtained a positive reaction in fifteen minutes after diluting the cerebro-spinal fluid eightfold, a phenomenon that certainly never occurs in the normal.

To sum up, we consider that we have in the Noguchi reaction and in the ammonium sulphate ring test two new methods of considerable value for readily recognizing an excess of globulin in the cerebro-spinal fluid, and thus for determining the presence of some parasyphilitic affection of the nervous system.

TREATMENT OF FACIAL PARALYSIS DUE TO MASTOID DISEASE OR TO THE MASTOID OPERATION.

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In the performance of a series of mastoid operations one is certain sooner or later to have the misfortune to divide the facial nerve during the course of the operation—it has occurred to me three times in over one hundred operations—as it may be found either completely exposed or surrounded by granulations, the curetting of which may completely sever it; or the paralysis may be present before operation, due to destruction of the nerve by the diseased process.

As far as I am aware, the treatment hitherto adopted has been facio-spinal accessory, or facio-hypoglossal anastomosis, the latter being the favourite. I have had two of the latter, and both were successful as far as recovery of the facial muscles was concerned; but the resulting disfiguring scar was objectionable, and the thought occurred to me of trying to join the two ends of the divided nerve in the course of the aqueduct of Fallopius at the site of injury. The following is a short summary of a case which was shown, together with one of my facio-hypoglossal cases, for the purpose of comparison at a meeting of the Stourbridge and District Medical Society on February 18th last:

John P., aged 5, admitted to the Walsall and District Hospital on May 12th, 1908, with chronic middle-ear suppuration and symptoms of cerebral irritation. The mastoid was opened on May 13th, and was found to be extensively diseased, a large part of the outer wall of the lateral sinus being covered with foul granulations. In following out the diseased bone the facial nerve was divided and recognized as such at the time of the operation, and upon recovery from anaesthesia the whole of the side of the face was completely paralysed. The operation was finished in the ordinary way, the wound being stitched up at the back, and the external meatus being thrown into the general cavity. The idea of end-to-end anastomosis occurred to me, and upon the second day after operation the child was again anaesthetized, the wound at the back reopened, the severed aqueduct exposed, and the proximal and distal ends defined, the distance between them being about from $\frac{3}{4}$ to $\frac{1}{2}$ in. As a scaffolding for the regenerating nerve silkworm gut was used, as it was thought it would better resist the phagocytic action of the tissues, and by its rigidity be more easily introduced into position, and retained there during subsequent dressings. A piece $\frac{1}{2}$ in. longer than the interval between the two openings in the bone was used, $\frac{1}{2}$ in. being inserted into each end of the bony canal. The case was dressed daily for a period of one month through the wound at the back, which was not again closed, mainly for convenience in dressing, but also for better drainage. The whole of the area of the anastomosis was carefully covered at each dressing with gutta-percha tissue to prevent any disturbance to the underlying silkworm gut, until the latter became covered with granulations. The battery was used from the first, but no movement of any kind could be produced by the patient for three months, when slight movements of the alae nasi of the affected side were observed upon forced sniffing, the other facial muscles afterwards gradually coming into use. The child was discharged on September 11th, with the wound epidermized and clean, a small fistula remaining behind the ear leading into the operation cavity. The boy has now recovered his normal expression when at rest, and when his facial muscles are thrown into action it is difficult to tell that there has been any facial paralysis at all.

I think I can lay claim to originality in this method of treatment, but I bring it forward for two reasons: first, because of the avoidance of an unsightly scar, which is no small matter in the case of a girl, and which is inevitable in the facio-hypoglossal method; and, secondly, because—as far as my experience of the latter operation goes—of the longer period of time taken for recovery of