The authorities were notified of this threat, but as he continued to pursue the even tenor of his ways, no steps were taken for his certification as a lunatic.

Four months after her admission the wife was sent out on trial, and three months later finally discharged as relieved.

A few weeks after she left the asylum she wrote me a letter, which clearly showed that she was still the subject of persecutory delusions.

Since then I have been unable to glean any further tidings of her, or to learn whether her hallucinations returned and were again communicated by her to her husband when she rejoined him.

In my opinion he would most probably never have suffered from delusions or hallucinations had he not been infected by his wife. Here we have the case of a simple unimaginative yokel married to a woman (in spite of the opposition of their respective families) to whom he was extremely attached, and whom he evidently regarded as both his intellectual and social superior.

It is not surprising that when she developed these delusions of suspicion against her own daughter and his, she should after some time have impressed him with their truth, or that by constant reiteration of her aural hallucinations by day and night after some months she should have succeeded in convincing him of their actuality.

Had not fate proved unkind in his second matrimonial venture, would not this ploughman have been content after his hard day's work to homeward plod his weary way and to leave the world, material and spiritual, to darkness and to—the poet?

(1) *Brain*, vol. x, 1888, p. 408.

Examination of the Cerebro-spinal Fluid as an Aid to Diagnosis in Certain Cases of Insanity, with Special Reference to the Protein Reaction described by Ross and Jones.(1)

By JOHN TURNER, M.B., Essex County Asylum, Brentwood.

THE value of Wassermann's reaction in the diagnosis of syphilitic and the so-called para-syphilitic diseases is now generally conceded, but, apart from the technical difficulties in carrying out the test, which places it beyond the means of all except those working in well-equipped laboratories specially licensed, the fact that it merely enables one to diagnose a previous syphilitic infection in nearly all its stages, detracts somewhat from its value as a means for the special diagnosis of general paralysis or tabes. Wassermann's reaction tells us what nearly every patient is able, if willing, to tell us; whereas the protein reactions, especially that described by Ross and

Jones, appear, so far at any rate as my observations go, to be much more specific in the information they yield. The Ross-Jones test in my hands only gave a positive result in general paralysis and *cerebral* syphilis.

1. *Protein Reactions.*

In 1909 Drs. G. W. Ross and E. Jones (1) described a very simple protein reaction, which consists in the addition of *clear* cerebro-spinal fluid to a *saturated* solution of ammonia sulphate, in such a manner that the fluid lies on the reagent without blending with it. In the case (according to these authors) of general paralysis, tabes, tertiary syphilis, and syphilis of the nervous system, at the junction of the two fluids a definite, sharply defined, thin white film, which has very much the appearance, when looked at against a dark background, of a cobweb, forms immediately or almost immediately. They believe that this reaction depends merely on the amount of globulin present in the fluid. Globulin, as we know, is present in normal cerebro-spinal fluid, but apparently in insufficient amount to give the reaction. I have carried out this test in the fluid from ninety-five cases of insanity, and my results would seem to show that it, especially in conjunction with a cell-count, affords most valuable help in making a diagnosis in early cases of general paralysis, and in differentiating certain early cases of alcoholic insanity from general paralysis. Although several of my cases had a history of recent or active syphilis, in only one case, syphilis of the nervous system, did I get a positive result except in general paralysis.

J. Henderson Smith and J. P. Chandler (2), writing of the Wassermann reaction, state that unfortunately in the *early* cases of general paralysis the reaction most often fails, and that even in the most advanced cases it is sometimes negative. In my experience the Ross-Jones reaction has *never* failed to give a positive result in early cases; agreeing to a large extent in this respect with the cell-count, which is usually most abundant in early cases, and which may be slight or even absent in older. In forty-eight cases of general paralysis, or suspected general paralysis, I only got a decided negative result twice: one was a case of seven years' standing, and from the clinical standpoint possessing no diagnostic difficulties; the other was a recent

case, æt. 2, of the real nature of which I am still in doubt. An advanced case of tabes with Charcot joints also gave a negative result.

All the cases (twelve) of dementia præcox, all the cases (eight) of alcoholic insanity, all the cases (eight) of epilepsy and all but one of seventeen cases not classified, including seven of secondary or organic dementia, gave a negative result. The exception gave a doubtful positive after twenty minutes. In ambiguous cases it frequently enables one to give with confidence a positive diagnosis which would without its aid be impossible. Three of the general paralytics were not diagnosed until after an examination of the fluid, although one of them had been an inmate five years, and another two years. On the other hand, three had been diagnosed as general paralytics, but the examination of the fluid indicated that this was incorrect. Two of these proved to be cases of polyneuritic psychosis, and the other a case of delusional insanity with paraplegic symptoms.

In the majority of the cases Noguchi's butyric acid test was employed also. This is somewhat more troublesome to carry out, and, so far as my experience goes, not quite so trustworthy as Ross and Jones, or perhaps one should say, not so specific, as it sometimes gives a positive reaction in cases of tertiary syphilis, and in three cases of general paralysis it gave a negative result, whereas the Ross-Jones test was only negative in one. This experience seems to coincide with Dr. G. S. Amsden's (3), who tested thirty-six cases at the Bloomingdale Hospital with Noguchi's, Ross and Jones's, and Nonne's phase 1 tests, and he found that the Ross and Jones method gave more definite and clear-cut results than Noguchi's, and that both were more sharp and delicate than Nonne's.

2. *Cell-count.*

The value of a cell-count for diagnostic purposes is scarcely, if at all, inferior to the protein reaction, and is especially useful, inasmuch as the number of cells is generally greater in early cases.

Joffroy and Mercier (4) state that the cytosis precedes the speech and pupil symptoms in general paralysis, and Frenkel (5) finds the same as regards the pupillary symptoms in tabes.

This aid to diagnosis, although largely used on the continent

and in America, has had far too little attention given to it in England.

I have followed E. Jones's (6) method, in which 3 c.c. of the fluid is centrifugalised for ten minutes and the supernatant fluid drawn off until only a fifth of the original bulk is left. As often with the clearest fluid erythrocytes are present, although quite invisible to the naked eye even after centrifugalisation, and, as these cannot be distinguished with certainty in counting, I add to the remaining portion of the fluid two small platinum loopfuls of a 1 *per cent.* solution of methl violet, which, after standing a few minutes, colours the leucocytes a pale blue, but does not stain the erythrocytes. The deposit is well stirred up and a few drops transferred to the Thoma-Zeiss counting-chamber in the usual way, and the field of the microscope is adjusted so that its diameter corresponds to 7·5 of the small squares in the counting-chamber, the area of the field being then $\frac{1}{90}$ mm. Three chambers are filled and thirty fields connected from each, and the total (ninety) represents the contents of 1 c.mm, but this has to be divided by five, as only one-fifth of the fluid was taken.

In fifty cases of general paralysis only six failed to show a cytosis (any number of cells below 5 per c.mm. being looked upon as negative). Three of these were chronic cases presenting well-marked clinical symptoms, two were recent cases and also well marked clinically; the remaining one was an acute case, in which several epileptiform seizures occurred the day before the puncture. In this case the diagnosis was confirmed by *post-mortem* and microscopical examination of the brain and cord four days later.

In forty-five cases of other forms of insanity only three showed a slight lymphocytosis. In one case of organic dementia with apopletic attacks the lymphocytosis was 8·8, in another it was 7·2, and in the third, a case of dementia præcox, 9·9 per c.mm.

As regards the differential count, the means were not at hand for carrying out Alzheimer's method, which involves centrifugalisation for one hour, and which is stated to give satisfactory results, and I must admit that the method I employed did not give entirely satisfactory results in all cases; occasionally there was some difficulty in differentiating between endothelial and plasma-cells.

Some of the deposit, after centrifugalising for ten minutes and drawing off all but a drop or so of the supernatant fluid, was spread on slides, dried and stained in Pappenheim's stain or else Leishmann's. But if the fluid is not treated before centrifugalisation, a very large number of pale, irregularly contoured bodies with badly defined or invisible nuclei are found in the deposit. They have the appearance of cells underlying a partial digestion or disintegration, and Pappenheim (7) found that especially in general paralysis the fluid does exert a very deleterious action on leucocytes, but this action can be destroyed by heating the fluid to 56° C. I found this to be the case, but eventually discarded the heating, which was troublesome, for the addition of two to three drops of 1 in 1,000 formalin. This entirely stops the disintegration of the cells, but produces a slight shrinking in them.

The total number of cells per c.mm. varies between very wide limits in general paralysis, generally somewhere between twenty and sixty. In three it was over a hundred.

The lymphocytes form the great bulk of all the cells present —from 80 to 95 *per cent.* In only a few cases were polymorphs noticed, and these were in fluids contaminated by blood at the time of puncture. I frequently, however, noticed quite large numbers of erythrocytes under the microscope from fluid which, even after centrifugalisation, appeared quite colourless to the naked eye.

The presence of plasma-cells from a perfectly clear fluid justifies a diagnosis of either general paralysis, tabes or cerebral syphilis.

Films were also stained in Unna's polychrome blue and examined for micro-organisms, which were found in seven cases, as follows:

Case 1.—Male, general paralytic. Swarms of diplococci (? pneumococci) occur in dense clusters, small groups, and singly. Also some slightly elongated diplo-organisms and a few longer and more slender diplo-organisms. This man was in fairly good health, and is still alive.

Case 2.—Male, general paralytic. An acute case. Death occurred a month or so after. No *post-mortem*. Numerous short, rod-like, beaded bacilli in clusters and short chains.

Case 3.—Male, cerebral syphilis; gummata of pons. Film crowded with diphtheroid organisms, similar to the preceding

case, and also pneumococci. Death a few months later. Autopsy.

CASE 4.—Female, epileptic imbecile. Film showed numerous tubercle bacilli and some streptococci. Patient still living.

CASE 5.—Female; alcoholic insanity (polyneuritic psychosis). Film crowded with diphtheroid organisms similar to those seen in the two general paralytics. Patient died five months later. Autopsy.

CASE 6.—Female, secondary dementia. Numerous diphtheroid organisms. Patient still living.

CASE 7.—Female; acute delirium. Film crowded with pneumococci. This last case was interesting. She was admitted April 23rd, 1909, in a state of low muttering delirium, and on October 22nd a blood-count was made, showing 8140 leucocytes per c.mm.; polymorphs, 63·25 *per cent.*; lymphocytes, 33·00 *per cent.*; hyalines 3·75 *per cent.* No eosinophiles. No organisms detected in blood. She died four days later from pneumonia and enteric. Some blood taken with aseptic precautions from the left ventricle sixteen hours after death was spread on serum and on agar tubes, and put into the incubator at 30° C.; the serum tubes remained sterile; the agar, after thirty-six to forty hours, grew two small round, yellow colonies of *Micrococcus tetragenus*, and one small, dull greyish-white colony of pneumococci.

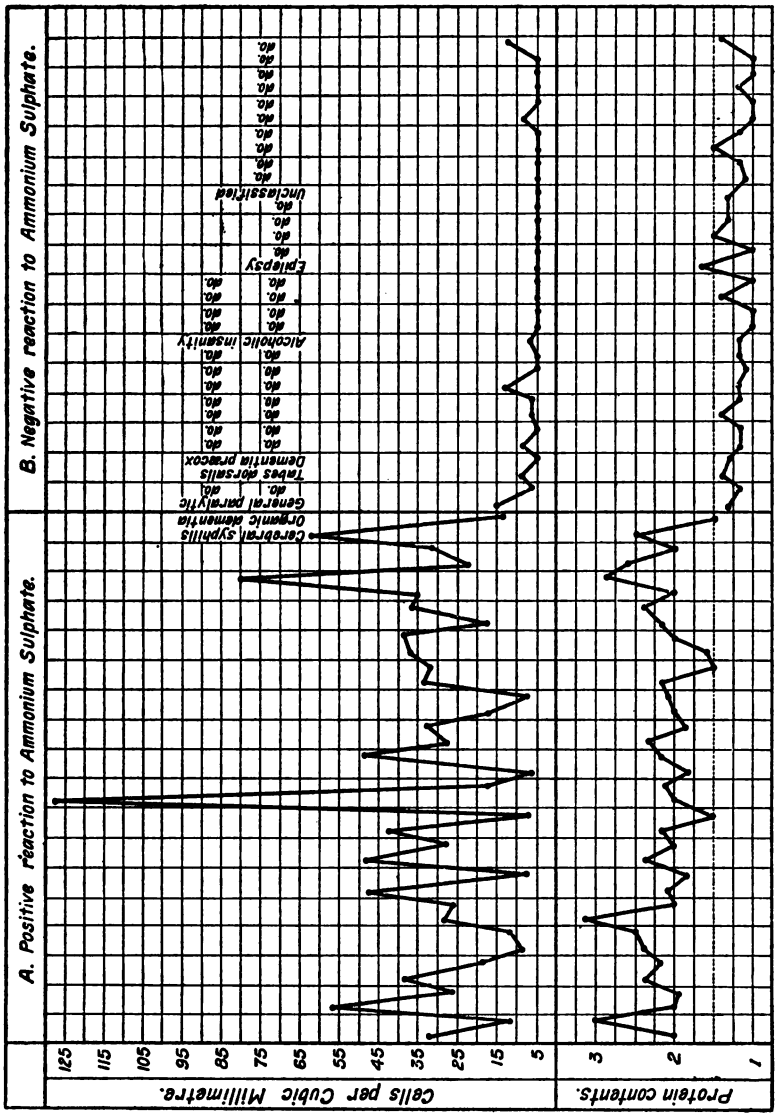
In two only out of twenty-one general paralytics were organisms similar to those described by Ford Robertson found, and they were found also in two cases not general paralytics.

3. *Total Protein Contents.*

A somewhat rough quantitative examination for the total protein contents was made by mixing 5 c.c. of the fluid with a like quantity of absolute alcohol, allowing the flocculent precipitate which forms to settle for two or three hours, centrifugalising for two minutes, again after the lapse of four or five hours, and again the next morning; by this time the supernatant fluid should be quite clear, and the precipitate forms a solid-looking mass at the bottom of the tube, and its height can be read off against the $\frac{1}{10}$ c.c. divisions marked on the tube.(3)

A glance at the table shows that a protein content over 1·5 on the tube is almost as characteristic of general paralysis as either the protein reaction described or the lymphocytosis.

All except two of the cases in this table reacting positively to ammonium sulphate had a protein content higher than 1·5.



The table shows at a glance the general correspondence between amount of protein in the fluid, the cytosis and the positive reaction to ammonium sulphate. All the positive cases except two were general paralytics. None of the negative except two were general paralytics. Although individual variations between the amount of protein and number of cells are very great, yet, with four exceptions, all the cases which show a high protein content also show a lymphocytosis, and all with a low content (below 1·5 degrees) show no, or a very slight, lymphocytosis.

These results lend considerable support to Ross and Jones's contention that the ring test depends merely on the amount of the protein contents. If this reaction, however, entirely

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depended on the amount of globulin in the fluid, it is difficult to account for a positive reaction in a few of the cases in which there was less protein than was found in two cases giving a negative reaction. According to my (8) experience, which I believe is borne out by most later investigators, practically the whole of the protein contents in the fluid of general paralytics is serum globulin. In twelve fluids which I tested fifteen years ago, after saturation with magnesium sulphate, no less than eight showed no trace of serum albumen on heating the clear filtrate, and only the very faintest trace in the other four. Purves Stewart (9), however, quotes two French observers (Guillam and Parant) as having found in sixteen cases of general paralysis that the clear filtrate, after saturation with magnesium sulphate, showed on boiling a characteristic precipitate (? serum albumen).

It might be supposed that organic brain lesions would be associated with an excess of protein in the fluid, and although to a very slight extent this was so in two out of four cases I examined, yet only one of these gave a (doubtful) positive reaction with ammonium sulphate.

J. Froude Flashman and A. Graham Butler (10) refer to this question; they found in three cases with extensive vascular cerebral lesions no evidence either of complement fixation or of increase in the total protein contents, which was only one-tenth the amount of that in the fluid of a general paralytic taken at the same time. They state that "there is no room for doubt that, apart from acute or subacute diseases, a heavy flocculent precipitate occurring in a cerebro-spinal fluid on the addition of a general albumen precipitant is very strong evidence that the fluid was derived from a case of general paralysis or tabes." This entirely coincides with my opinion.

4. *Reaction* (*Alkaline or Acid*).

In all the cases of this series, and in twenty examined fifteen years ago, I have obtained an alkaline reaction (and not amphoteric) to litmus paper, but with phenolphthaleine the great majority gave an acid reaction. The degree of acidity, however, is in many cases very slight. A very faint pink solution of phenolphthaleine was poured into two small beakers, so that the tint in both was similar in looking down at them as they

stood upon a porcelain slab. A little of the fluid was then added to one beaker, and generally the pink colour was immediately discharged. I found that fluid left unstoppered in my room, where gas is constantly burning, rapidly became alkaline, whereas similar fluid in stoppered bottles retained its acidity, and that in my later examinations where this source of fallacy was recognised and excluded, the results tend more and more to be uniformly acid with phenolphthaleine, but the *degree* of acidity varies greatly, and is most marked in case of general paralysis.

Dr. A. Connal (11), testing the reaction to phenolphthaleine of the fluid in infective diseases of the meninges, found an *alkaline* reaction in all. He states that normal fluid possessed the highest and turbid fluid the lowest degree, and lessened alkalinity was found to coincide with disappearance of the dextrose (copper-reducing substance) normally present. Boiling a turbid fluid with Fehling invariably failed to reduce the copper, and this absence of reduction was further associated with the presence of lactates as tested for by Uffelmann's reagent.

I tested some of my cases for lactic acid by Uffelmann's reagent, using 5 c.c. and counting the number of drops of fluid required to decolourise it, and I found in four cases of general paralysis from 30 to 45 drops were needed, in two epileptics 40 and 42 respectively, in one case of acute delirium (with enteric) only 25 and in one alcoholic case no less than 90 drops. After death the decolourising power rapidly increases, so that 12 or 13 drops are sufficient. And also after death, as I pointed out fifteen years ago, the copper-reducing substance rapidly disappears from the fluid.

5. *Copper-reducing Substance.*

This substance, which at different times has been asserted to be sugar, pyro-catechin, dextrose, one of the purin bases, and recently, by Dr. G. S. Williamson (12), glucosamine, the reducing body of mucus, was tested for with Fehling's solution in 73 cases (58 in this series and 15 in my first series fifteen years ago). During life it was only found to be absent on two occasions, and both of these were in advanced general paralytics.

These results do not coincide very closely with Williamson's, who found it to be absent in 14 out of 22 general paralytics, and he stated that the reaction is as constantly absent in the early as in the late stages.

In 51 cases the amount of copper reduced was estimated quantitatively, and it was found that the amount was least in general paralysis and greatest in alcoholic insanity.

Thus in 21 general paralytics it averaged 16·4 (in 10 c.c. of fluid); in 7 epileptics, 19·0; in 10 (unclassified), 19·8; in 6 cases of dementia præcox, 21·3; in 5 of alcoholic insanity, 22·2 mgrm.

The rapid disappearance of this substance after death is striking, and, so far as my experience goes, constant; for example, in a male general paralytic in whom during life it was abundant, it was entirely absent eight and a half hours after death, which occurred sixteen days after it had been tested for during life. In another, where during life 10 c.c. of fluid reduced 22 mgrm. of copper, it was absent thirteen and a half hours after death, which occurred fourteen days after the first examination.

In another, where during life 10 c.c. reduced 15 mgrm. of copper, it was absent seventeen hours after death, seven weeks later. In two cases of dementia præcox of the katatonic form, where during life it was present, it was found to be absent after death, which occurred eight days later in one case and five days in the other.

In one case where the fluid was tested only four hours after death a slight amount was present; probably in this case a long enough time after death had not elapsed for all of it to be got rid of.

J. H. Coriat (13) found it in 9 out of 29 cases in the *post-mortem* fluid, but in the account from which I take this information no mention is made of the time after death that the fluid was tested. Probably, as A. Connal points out, this disappearance of reducing substance is due to, or at least associated with, the presence of lactates in the fluid, for after death, if one may trust the Uffelmann reagent, the amount of lactic acid rapidly increases. To give an example, one case in which during life thirty drops of fluid were required to decolorise 5 c.c. of the reagent only required thirteen drops one hour after death, which occurred two days later (3).

6.

I will just briefly touch upon some of the interesting features noticed in the cases other than general paralysis or cerebral syphilis which were examined.

A. *Dementia Præcox.*

The fluid was examined in 12 cases (4 hebephrenics, 7 katatonics and 1 paranoidal), and all gave a negative result with the Ross and Jones test. Two gave a slight lymphocytosis, 4·5 per c.mm. and 9·9 respectively. Two of the subjects had had syphilis. In one of these, infected two years ago and under treatment in the asylum, but not during the last nine or ten months, the Noguchi reaction was positive; in the other, infected six years ago and treated for a year (according to her own account), the Noguchi reaction was not tried.

In several of the cases the fluid came away rapidly, in nearly confluent drops, and in one of these cases, a woman in a stuporose condition, there was a marked mental improvement a few hours after the puncture. She had been subject to stuporose attacks with lucid intervals for some years, but latterly the attacks had become much longer and the lucid intervals very short. The improvement after the tapping, however, lasted for six months. She then again relapsed and was again tapped and 13 c.c. of fluid removed (on the previous occasion 20 c.c. were taken). Two days later she emerged from her stuporose state and became cheerful and communicative, but this improvement coincided with a short attack of subacute rheumatism and only lasted two days.

In another case which had been persistently stuporose for nearly two years no improvement followed the withdrawal of 20 c.c. of fluid. In this case the fluid came away slowly.

B. *Epilepsy.*

Four men and four women were punctured; all the women and at least three of the men were imbeciles. The only points to which notice need be directed are that in one case suffering from tertiary syphilis with destruction of soft palate (not under treatment) a positive reaction was obtained with Noguchi's

reagent, a negative with ammonium sulphate; and in two cases there was a rather high protein content, 1·5 degrees in one (the syphilitic case) and 1·7 in the other.

c. *Alcoholic Insanity.*

The fluid from seven women (all examples of polyneuritic psychosis) and one man (a doubtful or impure case) was examined. Beyond the fact that the copper-reducing substance in two was present in large amount (and it is worth noting that in both of these the reaction to phenolphthaleine was alkaline) it presented normal characters, gave negative protein reactions and contained no excess of cells.

In six of the women the puncture was made shortly after admission to the asylum, and during an early stage of the disease; the remaining case had been an inmate for three years.

In early stages it is often impossible, apart from an examination of the cerebro-spinal fluid, to make a positive diagnosis between this disease and general paralysis. In these doubtful cases the information obained from the examination of the spinal fluid is invaluable, and permits a positive diagnosis being given—a matter often of the greatest practical utility.

It should, however, be noted that Nissl (14) cites two cases of *chronic alcoholism* with positive cytological result.

After-Effects of Lumbar Puncture.

Nissl (14), in 1904, pointed out that even after the withdrawal of only a few c.c. of the fluid, symptoms similar to sea-sickness were frequently met with—headache, nausea, vomiting, pains in back and neck, and a feeling of apathy—which occurred only after five to six hours, and were not experienced in the recumbent position. They lasted from one to eight days, but no permanent damage, according to him, resulted.

Several of my cases complained of similar symptoms, together with a feeling of constriction about the chest, but in all these symptoms were slight and transient, and no permanent ill-effects have followed the operation.

Summary.

The main points of practical interest in the examination of the cerebro-spinal fluid are the protein reactions and the cell-count. Both are of great value for the early diagnosis of general paralysis, tabes, or cerebral syphilis.

The simplicity of the Ross and Jones test brings it within the reach of any qualified man, and it would appear to be the most delicate of all the protein reactions.

So far as I know this series is the largest in which the reaction has been tested. Ross and Jones only tested 27, and Amsden 36 cases.

At the present time the other characters noted, the acidity or alkalinity and the presence of copper-reducing substance, are mainly of academic interest. It is probable, however, that the degree of acidity to phenolphthaleine may coincide with the development of lactic acid in the fluid during life, and this with the disappearance or lessening of the copper reducing substance; so that inasmuch as lactic acid is rapidly formed in dying nervous tissue, we may have here the means of establishing a test as to the extent of the organic nervous changes in any given case.

Writings on the subject of the spinal fluid are now so numerous that some apology is almost needed for adding to their number, especially when, as in my case, nothing new is recorded. Still, I felt it was worth while further testing the trustworthiness of such a simple reaction as that described by Ross and Jones, by its application to a larger number of cases than has hitherto been done, and from my results it appears to come successfully out of the ordeal.

Note Concerning Cadaveric Cerebro-spinal Fluid.

Smith and Chandler (2) state that fluid from bodies kept in the cold room (at Claybury) is as clear and limpid as in life. I have, however, always found that when the corpse remains at ordinary temperature, even in winter, the fluid becomes turbid and quite unsuitable for the Ross-Jones test a very few hours after death, and at the same time it is found to contain very many large, ill-defined cells—as many as four hundred or more per c.mm. For example, in two cases of dementia præcox, in

neither of which the fluid contained any cells during life, they were found in very large numbers after death, which occurred six and eight days later respectively.

(1) A paper read at the Quarterly Meeting, held in London May 24th, 1910.—(2) Care should be taken to ascertain by a standard 1 c.c. pipette that the markings on the tube are correct. I had to discard several of my findings in earlier cases from not paying attention to this point, for very considerable inaccuracies were found in the markings on the tubes which had been used.—(3) This only applies to fluid removed from a cadaver. Fluid taken during life does not alter in respect to its decolourising power on Uffelmann's reagent however long it is kept, provided it remains undecomposed.

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Discussion,

At the Quarterly Meeting held in London on May 24th, 1910.

The President thanked Dr. Turner on behalf of the meeting for his paper, which he regarded as of extreme value.

Dr. Hubert Bond said he could quite corroborate the statement with regard to the ease with which the test was applied. At Long Grove Asylum they had recently been using it. He hoped to hear of some equally ready test to reveal cases which at some period of their lives had had syphilis. The Wassermann test was difficult, could only be done in certain laboratories, and by those trained in the technique. While the test described by Dr. Turner was easy and within the scope of all asylums, it would seem that it yielded information only with regard to syphilis of the nervous system. Whereas, bearing in mind the vitiating power of syphilis on the system generally, it becomes more and more of importance to be able to say definitely how many of our asylum cases have at some time contracted the disorder.