

*Further Investigation on the Cerebro-Spinal Fluid in Insanities.* By G. SCOTT WILLIAMSON, L.R.C.P., and J. R. P. PHILLIPS, M.R.C.S., Assistant Medical Officer, City and County Asylum, Fishponds, Bristol. (From the Pathological Laboratory of the Bristol General Hospital.)

PART I.

By G. SCOTT WILLIAMSON.

THE investigations recorded in the following paper were undertaken to determine the reason for the discrepancy in the results when applying the Wassermann reaction to the cerebro-spinal fluid and blood-serum of general paralytics. The experiments have yielded results significant in other directions which are of some interest.

The cerebro-spinal fluid yields a positive Wassermann reaction in 97 or 98 *per cent.* of cases, whereas only about 50 *per cent.* of cases give a positive result when the test is applied to the blood-serum.

What hypothetical explanation can be offered to explain this difference?

It may be that there is a purely local infection yielding (*a*) an immune body in the cerebro-spinal fluid only, or (*b*) an immune body in great concentration in the cerebro-spinal fluid with only traces in the blood-serum. This is conceivable but hardly probable. The Wassermann technique is, however, a very delicate test for the presence of immune body, and would detect any mere difference in concentration and quantity.

To explain the 50 *per cent.* of positive cases under the first assumption there would require to be some second focus of infection. Moreover, if general paralysis of the insane is an infective process in which the response to a toxic agent is confined to an area without a general participation, it would stand isolated as contrary to all experience in other toxic conditions.

The histo-pathology of general paralysis of the insane has not yet demonstrated any clear distinction between the perivascular changes in the brain and meninges and those in the other organs in that disease. From these considerations it

would seem necessary to seek some other less simple explanation.

Another hypothesis accepts the condition of a general toxæmia and response, and seeks the explanation in the chemical constitution of the cerebro-spinal fluid in general paralysis of the insane.

Paghini and others have emphasised the constant increase in the amount of the cholesterol bodies in the cerebro-spinal fluid of general paralysis of the insane, and further, the phosphatides are very variable quantities in cerebro-spinal fluid. In the blood-serum the lecithins are undoubtedly increased, whereas I have been unable to detect any appreciable increase in the cholesterol content. Muir, Mackenzie and Browning have fully demonstrated the effect of the compounds in mixtures yielding a positive Wassermann, and their influence upon hæmolytic bodies is well known. The exact significance of these considerations is at present under consideration.

During these investigations it became necessary to detect the presence of blood-serum in the cerebro-spinal fluid. For this purpose advantage has been taken of the presence in blood-serum of a ferment capable of splitting a synthetic di-peptide, glycol-tryptophane, into its two components. This ferment is not present in normal secretions, *e.g.*, cerebro-spinal fluid, synovial fluid, etc. It does appear in these fluids under the stimulus of a local irritant.

The following normal cerebro-spinal fluids have been tested, and found free from ferment.

A cerebro-spinal fluid is classified as normal when it yields a uniform amount of protein, ash, nitrogen, and contains a reducing body in from 0.035 to 0.043 *per cent.*, urea in from 0.009 to 0.046 *per cent.*, and does not contain fibrinogen, albumose, or albumen. Sixteen such fluids have been tested from 5 cases of accidental death, 4 cases of cardiac disease, 2 cases of carcinoma of viscera, 2 cases of hysteria, 1 case of Addison's disease, 1 case of sunstroke?, 1 case of chorea.

This would seem sufficient evidence to justify the assumption that cerebro-spinal fluid is not a transudation, but a specific secretion (see Table). Further evidence of this is got from the fact that animals whose blood-serum contains a high concentration of agglutinins in artificial immunity do not yield a cerebro-spinal fluid that agglutinates.

Cerebro-spinal fluid from the following cases gave a positive ferment test, though some of them only differed from the prescribed standard of chemically normal fluids in the slightest degree: 4 cases of tuberculous meningitis, 4 cases of tabes dorsalis, 3 cases of uræmia, 3 cases of malignant endocarditis, 3 cases of septic meningitis, 2 cases of diabetes, 2 cases of typhoid fever, 2 cases of secondary syphilis, 2 cases of hydrocephalus, 1 case of rheumatic fever, 1 case of pneumonia, 1 case of spinal caries, 1 case of optic atrophy, 1 case of fibroma of dura-mater.

Thus there is exudation of serum in these irritative conditions, the lesions being general or local. Uræmia, diabetic coma and pneumonia may be counted as pure toxæmias; rheumatic fever, typhoid fever, etc., as septicæmias; while the case of fibroma of the dura with paralytic symptoms represents a purely local irritation.

In the normal cerebro-spinal fluids exception may be taken to chorea as being an undoubted irritative condition; it must be remembered, however, that chorea, as far as the symptoms go, could be well classified as a pure peripheral nerve lesion. One case cannot, however, furnish matter for argument.

It seems probable, then, that the presence of this ferment in cerebro-spinal fluid means an irritative transudation, though not necessarily inflammatory. The continued presence of this ferment would mean a progressive irritation.

Viewed in this light, the cerebro-spinal fluid from cases of insanity yields some interesting results.

Every cerebro-spinal fluid giving a positive Wassermann reaction contains this ferment without exception.

The most striking result is the overwhelming number of positive ferment tests. Of fifty-two fluids examined only eight gave no evidence of this ferment.

The condition of these patients will be dealt with later; suffice to say at present that they represent cases in which it is absolutely certain there is no progressive irritation present and for the most part are imbeciles. When it is borne in mind that these tests were performed in ignorance of the condition of the patient yielding the fluid, and that out of fifty-two cases these eight were picked out, it goes far to prove that the presence of this ferment is coincident with irritation and the significance of the remaining forty-four cases is considerable.

For if there is a persistent irritant, there is something under-

lying some insanities that can be dealt with either by removing the cause or opposing and counteracting the effect, in other words we must treat and not palliate insanities, and this furnishes yet another inducement to the prosecution of research into the ætiology of insanity.

Another explanation is possible. The irritant may not be persistent, but the effect remains which establishes a vicious circle, the psychic import of which yields a mental explosion that mechanically leads to a hyperæmia with transudation: in other words it is not cause, but effect, with which we have to deal. The only proof of the latter is by exclusion of the former.

English psychologists generally adopt the psychic explanations without proof, and seek (curiously enough) to palliate or cure by a sociology repugnant to all but the most advanced materialists. Therein the paradox seems complete.

#### Appendix.—*The Glycol-Tryptophane Test.*

*Solution required.*—1. Glycol-tryptophane, sold as “Ferment Diagnostium” by Kalle, of Biebrich.

2. A solution of bromine water, 3 parts; glacial acetic 10 *per cent.*, 5 parts.

3. Toluol.

Five to 10 c.c. cerebro-spinal fluid measured into a test-tube, and 1 c.c. glycol-tryptophane solution added and covered with toluol. Incubate for twenty-four hours at 37° C.

Take out a sample, and add the bromine water drop by drop until a rose-pink or lilac colour appears, disappearing on further adding bromine water.

The appearance of a lilac or rose-pink colour indicates free tryptophane and a positive reaction.

*Note.*—This communication is merely a preliminary report upon work in progress, and any deduction drawn from the facts must be of a purely tentative nature, or, at least, in no wise dogmatic.

## PART II.

By J. R. P. PHILLIPS.

THE prime object in examining a short series of cerebro-spinal fluids was to arrive, if possible, at an independent opinion of the Noguchi reaction as a simple bedside means of recognising the changes in the cerebro-spinal fluid due to syphilis, and to compare it with the Wassermann test. A satisfactory conclusion has resulted, and we appear to have lit upon some suggestive incidents by the way. First, reference will be made to the technique and methods of procedure before giving results and subsequently showing a few cases. In making the necessary lumbar punctures, after taking the usual antiseptic precautions,  $\frac{1}{2}$  c.c. of eudrenine was injected beneath the skin into the subcutaneous tissues and allowed to act for four minutes.

The escaping fluid was caught in a sterilised bottle, and after Noguchi's test had been done, and the result recorded, the bottle was labelled with a number only, and sent to the laboratory. No comparison of results was made until after forty fluids were independently examined, and none again until after the examination of the remaining number. Fluid has been examined from nearly every male general paralytic or suspected general paralytic up to a recent date, a patient in this asylum—20 cases; in 14 of these the immediate Noguchi test, the laboratory test and Wassermann's reaction all gave corresponding results. Of 3 suspected cases, one will be shown directly, one is dead, and showed no *post-mortem* changes suggestive of general paralysis, and the third has unfortunately been transferred to another asylum. The three cases were all negative to all three tests, and so helped to eliminate general paralysis. A fourth case, a suspected general paralytic, which is also shown, was, at two separate punctures, negative to both the Noguchi's, on the first occasion gave a positive Wassermann and on the second a negative Wassermann.

So far the laboratory results and the immediate examinations are in absolute accord, and the Noguchi and Wassermann reactions are also in accord with one exception.

There remain two cases, one clinically and *post-mortem* a typical general paralytic, and the second also clinically appa-

rently a strongly marked general paralytic; these were both positive Noguchi's at the bedside and negative to both laboratory tests. The latter case, however, is attributed possibly to the fluid having become accidentally contaminated by bacteria in transit.

In 95 *per cent.*, then, of cases the Noguchi reaction seems to have shown itself a perfectly reliable, simple, clinical test, and in absolute accord with the laboratory Wassermann technique.

The bulk of the remaining cases were taken haphazard for purposes of comparison. As to the ferment reaction, this gave a positive result in all general paralytics, alcoholics, and numerous others in which the clinical symptoms were acute or progressive, but in the majority of cases in which the symptoms were non-progressive there was a negative result.

In two cases, however, it gave a positive result, although the patients had settled down quietly for years with no apparent increase of dementia. Amongst the whole series a type has been met with apparently having characteristics of its own in relation to lumbar puncture. These are the youthful congenital imbeciles. There are four of these in the series. They all bore the puncture perfectly well, expressing neither fear, reluctance, nor pain. They were all attacked within a few hours by more or less persistent vomiting, a varying degree of frontal headache, vertigo on attempting to rise, and slight malaise. There was no apparent change in their mental state. These were imbeciles of a mild type and fairly intelligent. Their symptoms, as shown by their charts, were unaccompanied by any fever, so that one may exclude sepsis. There was a brief rise in the course of one chart, which is, however, attributable to an intermittent condition. They were, with one exception, in bed for some days, and though repeated attempts to get them up were made, the vomiting, whilst not occurring in the horizontal, returned on assuming the vertical position. The quantity of fluid withdrawn in all cases never exceeded 50 c.c., and would not average 20 c.c. In searching for a possible cause of these symptoms it is possible that the explanation is some interference with the semicircular canals, and that the only way in which these might be so affected appears to be through a patent ductus endo-lymphaticus. This duct communicates, on the one hand, with the membranous labyrinth of the internal ear, and, on the other hand, is said to end blindly in the posterior surface

of the petrous portion of the temporal bone in the substance of the dura mater.

The ordinary text-books on anatomy make very little reference to this structure, and Dr. E. Fawcett, Professor of Anatomy, Bristol University, states that so far as is known from reference to text-books such is the case. It has been suggested that the

TABLE I.—Including all those Cases in which the Wassermann Test gave a Positive Reaction.

No.	Diagnosis.	Duration.	Excited.	Noguchi.	Wassermann.	Peptase.	Chemistry.	Post-mortem.	Remarks.
1	General paralysis	10 mths.	—	+	++	+	ab.	—	—
2	Ditto	1 year	+	++	++	+	—	—	—
5	"	"	+	+	+	+	—	General paralysis	—
6	"	"	—	+	+	+	—	Ditto	—
11	"	2 years	—	+	+	+	—	—	—
12	"	"	—	+	+	+	—	—	—
14	"	3½ years	—	+	+	+	—	—	—
21	"	2½ years	—	+	+	+	—	—	—
28	"	9 mths.	+	+	+	+	—	—	—
29	"	2½ years	—	+	+	+	—	General paralysis	Female.
32	Secondary dementia	11 years	—	+	+	+	—	—	Has a perforated palate.
34	General paralysis	9 mths.	+	+	+	+	—	—	—
37	Ditto	1½ years	—	+	+	+	—	General paralysis	Double optic atrophy.
20	"	9 mths.	—	—	+—	+	—	—	Varying results with Wassermann on separate occasions.
9	"	"	—	+	++	+	—	—	—
47	Congenital imbecility	From birth	—	+	+	+	—	—	A moral imbecile with fair physical development.

symptoms may be due to occlusion, complete or partial, of the foramen of Majendie preventing the escape of the cerebro-spinal fluid from the ventricles into the subdural space, and so giving rise on withdrawal of fluid from the latter to a certain amount of pressure and irritation, either on the floor of the fourth ventricle or on the cerebellum, or both.

It would be difficult in the latter case to suppose :

(1) How the withdrawal of so small an amount could cause an irritation lasting over so long a period.

(2) Why, with the patient in the recumbent position, no vomiting or vertigo occurs?

(3) Why, if due to an irritation of the vomiting centre

TABLE II.—Including Cases giving a Positive Peptase and a Negative Wassermann Reaction.

No.	Diagnosis.	Duration.	Excited.	Noguchi.	Wassermann.	Peptase.	Chemistry.	Post mortem.	Remarks.
3	Secondary dementia	19 years	—	—	—	+	—	—	—
4	Mania	7 years	+	—	—	+	—	—	—
7	"	10 months	+	—	—	+	ab.	—	—
8	Alcoholic Melancholia	7 months	+	—	—	+	—	—	—
13	"	12 years	—	—	—	+	ab.	—	—
15	General paralysis	1 $\frac{5}{8}$ years	+	—	—	+	ab.	General paralysis	Bedside Noguchi + laboratory Noguchi —
17	Mania	2 months	+	—	—	+	—	—	—
18	Progressive dementia	4 $\frac{1}{2}$ years	—	—	—	+	—	—	At first a suspected general paralysis.
19	Melancholia	5 months	+	—	—	+	—	—	—
22	"	3 months	+	—	—	+	—	—	—
23	Stupor	7 months	+	—	—	+	—	—	—
24	Mania	9 years	+	—	—	+	—	—	—
25	"	1 $\frac{7}{8}$ years	+	—	—	+	ab.	—	—
27	General paralysis?	5 months	+	—	—	+	—	—	Transferred to another asylum.
30	Stupor	1 $\frac{1}{2}$ years	+	—	—	+	—	—	—
31	Melancholia	11 months	+	—	—	+	—	—	—
33	"	1 $\frac{4}{8}$ years	+	—	—	+	—	—	—
35	Alcoholic Dementia	4 $\frac{9}{8}$ years	—	—	—	+	—	—	—
36	"	14 years	+	—	—	+	—	—	—
39	Congenital imbecility	from birth	+	—	—	+	—	—	—
40	Alcoholic Epileptic	2 $\frac{1}{2}$ years	+	—	—	+	—	—	—
41	"	13 years	+	?	—	+	ab.	—	Bedside Noguchi negative.
42	"	12 years	+	?	—	+	—	—	Ditto.
46	"	14 years	+	?	—	+	—	—	"
52	General paralysis	6 months	+	—	—	+	—	—	Bedside Noguchi positive.

in the medulla caused by an increased pressure tension, other centres in the same region are not equally affected?

All points being considered, then, it appears probable that a patent ductus endo-lymphaticus occurs in these cases. If this is an abnormality, and the text-books supply little for or



against such assumption, it is in keeping with other congenital aberrations associated with such cases, *e.g.*, patent ductus arteriosus, etc.

In the annexed tables the figure in the first column is merely for reference to case-books. In the fourth column, headed "excited," a + sign indicates active excitement, either maniacal or melancholic, at the time the cerebro-spinal fluid was obtained, a - sign the absence of such excitement.

In the columns headed "Noguchi," "Wassermann" and "peptase" + equals a positive, - a negative reaction; where two signs are placed opposite the same number, as ++, it indicates a very strong reaction. In Case No. 20, Table I, the cerebro-spinal fluid was tested at an interval from two separate punctures.

TABLE III.—Including those Cases giving a Negative Reaction to both Wassermann and Peptase Tests.

No.	Diagnosis.	Duration.	Excited.	Noguchi.	Wassermann.	Peptase.	Chemistry.	Post-mortem.	Remarks.
10	Congenital imbecility	From birth	-	-	-	-	-	-	-
26	Ditto	"	-	-	+	-	-	-	-
38	"	"	-	-	-	-	-	-	-
43	"	"	-	-	-	-	Normal	-	-
50	Progressive dementia	2 years	-	-	-	-	-	-	-
51	Congenital imbecility	From birth	-	-	-	-	-	-	-
44	Epilepsy	Over 15 years	-	-	-	-	Normal	-	-
45	Epileptic	4 years, probably longer	-	-	-	-	"	-	-

### Occasional Notes.

*British Medical Association, Annual Meeting, 1911.*

The Section of Neurology and Psychological Medicine held a series of highly successful meetings under the Presidency of Dr. Edwin Goodall in Birmingham in July last.