THE CORRELATION OF CLINICAL AND SERO-
LOGICAL FINDINGS IN PARESIS AND
CEREBROSPINAL SYPHILIS.*

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Considerable interest has, of late, been attached to the value of the Wassermann reaction in the differential diagnosis of general paralysis of the insane and cerebrospinal syphilis, and there appears still to be some divergence of opinion. In 1909, Ernest Jones¹ summed up the literature relative to general paralysis to date by saying: "A positive reaction (Wassermann) in the cerebrospinal fluid is strongly indicative of general paralysis, a negative reaction less strongly but unquestionably indicative of its absence; a positive reaction in the blood serum of a suspected case of general paralysis is of some value in support of the diagnosis, a negative reaction there is of much greater value in excluding such a diagnosis." Although many report 100 per cent positive findings in both blood and fluid, the above general statement is to-day probably more acceptable to the majority of workers than any more rigorous insistence upon constantly positive results. Nonne, in his book states: "Positive W. R. in the blood means no more than that the person has once been in contact with syphilis (hereditary or acquired), or that somewhere in the body a specific lesion still exists, but it does not mean necessarily that the disease in question must be luetic." And relative to the spinal fluid: "In the large majority of cases of general paralysis the W. R. is usually positive on using only 0.2 cc. of fluid, but in some few cases, and in most cases of cerebrospinal syphilis and of tabes, the W. R. is positive only on using larger quantities of cerebrospinal fluid." As typical findings he gives the following:

General paralysis:

Blood positive in 100 per cent.

Fluid positive in 90 to 100 per cent.

Cerebrospinal syphilis:

Blood positive in 70 to 80 per cent.

Fluid positive in 20 to 100 per cent.

* From material collected at the Warren State Hospital.

In these instances the smaller figures are for technique in which small amounts of the serum or fluid have been employed and the larger for that in which more is used. Several American writers, notably Kaplan, have insisted on the value of a negative W. R. in the cerebrospinal fluid in the differential diagnosis. He makes the following statement,³ which perhaps represents the extreme viewpoint. "It is possible to differentiate serologically between paresis and cerebrospinal syphilis," and tabulates the difference as follows:

General paralysis:

Blood W. R. positive (rarely negative).

Fluid W. R. positive (rarely negative).

Cerebrospinal syphilis:

Positive or negative.

More often negative.

While examining the opinions given at staff meetings at the Warren State Hospital on 697 routine admissions, it was found that 87 (12.5 per cent) were considered to be syphilitic diseases. Of these 69 (9.9 per cent) were, in the opinion of the majority, unquestionable cases of general paralysis and 5 (0.7 per cent) were cerebrospinal syphilis. Concerning the remaining 13 cases (1.8 per cent) there was a diversity of opinion. By a more careful analysis of these cases it was determined that eight of the 69 paretics had had negative Wassermann reactions upon the blood, this being 11.6 per cent of all those suffering from this disease. Three, or 60 per cent of the cerebrospinal syphilitics also failed to show a positive reaction on the blood. In all these cases the W. R. on the spinal fluid was positive. As the value of such observations as these depends almost entirely upon the accuracy of the Wassermann technique I will quote the following from Paul G. Weston⁴ as that used by him in all the cases reported here:

Wassermann Reaction.—The quantities of all reagents used were half those ordinarily used in the Wassermann test.

Complement.—The mixed serum from five guinea pigs was used. It had been three hours on the clot, one-half hour at 37° C., and two and a half hours at 5° C.

Hemolytic Amboceptor.—Antihuman rabbit was used. The unit was the amount that would cause complete hemolysis of 0.5 cc. of a 2.5 per cent suspension of washed human corpuscles in the presence of 0.05 cc. of the above described complement in a 2.5 cc. mixture in just two hours at the temperature of 37° C. Two units were used in each test.

Positive Control Serum.—Serum obtained from a case of paresis was used. It was inactivated by heating in a water bath at 55° C. for one hour.

Negative Control Serum.—A mixture of sera obtained from 10 non-syphilitics was used. It was inactivated by heating in a water bath at 55° C. for one hour.

Antigen.—Human heart muscle, free from pericardial fat, was ground in a meat chopper and covered with absolute alcohol in a wide-mouthed bottle. After 48 hours the alcohol was decanted onto a dinner plate and the tissue expressed between layers of cheese cloth. The expressed juice was added to the alcohol and the tissue returned to the bottle. The alcohol was evaporated by means of a current of air from an electric fan and the residue scraped up with a bone spatula and added to the tissue. Three volumes of absolute alcohol were then added and the bottle remained at room temperature for two weeks. At the end of this time the alcoholic extract was filtered off and to each .8 cc. was added 2 cc. of a 2 per cent solution of cholesterol in absolute alcohol.

Titration.—This antigen was non-hemolytic. The anticomplementary dose with normal serum was .15 cc. The antigenic dose was .00125 cc. The amount used in each test was .0125 cc. or 10 times the least antigenic dose, and one-twelfth of the anticomplementary dose.

Controls were carried for each reagent.

Spinal Fluid.—In all reactions 0.5 cc. of unheated fluid was used. The globulin was tested according to the method of Noguchi.

Cell counts were made by the Fuchs-Rosenthal method. Five drops from each pipette were counted.

All the reactions mentioned as positive were + + + +.

As the number of cases observed here is small, it seems worth while to present somewhat in detail those in which the laboratory findings are of the most interest.

CASES DIAGNOSED PARESIS IN WHICH BLOOD W. R. WAS NEGATIVE.

CASE No. 1, HOSPITAL No. 6834.—Patient male, aged 43, laborer. History of syphilis "many years" ago. Psychosis began when 40 years old with abrupt change of disposition, morose manner, talkative and expansive delusions. Physical examination showed equal, irregular, spastic pupils, unequal knee reflexes, sensory disturbances, incoordination, slurring speech and washed out facial expression. The one specimen of the blood taken was negative to the Wassermann. Of eight spinal fluid examinations the Wassermann reaction was seven times positive and once negative. Globulin positive once, negative seven times and the cells varied from 13 to none. Death occurred two years and eight months after the onset. At the post-mortem examination the diagnosis of paresis was confirmed.

CASE No. 2, HOSPITAL No. 8201.—Patient male, age 46, lumber dealer. History of syphilis six years ago. Five months before death he became irritable and complained of indefinite illness. Six weeks later he suddenly

became much confused, had vivid visual hallucinations, strong auto-accusatory trend of thought and delusions of persecution. During his hospital residence of two months consciousness was clouded, disorientation was complete, and he was restless, conversed incoherently and expressed many vague changeable delusions of a persecutory and somatopsychic nature. Physical examination showed muscle tremors, incoordination, slurring speech, areas of anæsthesia, Argyll-Robertson pupils, hyperactive knee reflexes and relaxation of the facial muscles. One specimen of the blood and fluid was taken. Wassermann reaction negative in the blood, positive in the fluid. Globulin positive and cell 40 per cubic millimeter. Two months after admission death occurred and the autopsy confirmed diagnosis of paresis.

CASE No. 3, HOSPITAL No. 8066.—Patient male, age 44, musician. History of syphilis when 36. Psychosis began when 41 years old with failure to attend to his work, forgetfulness, delusions of grandeur, and gradual general mental delapidation. Physical examination showed positive Romberg, muscle tremors, Argyll-Robertson pupils, hyperactive unequal knee reflexes, slurring speech and washed out facial expression. Two specimens of blood were negative to the Wassermann test but after a .45 gm. dose of neo-salvarsan, with Swift-Ellis treatment seven reactions taken over a period of two years were positive. Eleven specimens of the fluid were all positive to the Wassermann; eight were positive and three negative to the globulin test and the cells varied from 70 to none. Death occurred two and a half years after admission and the autopsy confirmed diagnosis of paresis.

CASE No. 4, HOSPITAL No. 8195.—Patient male, age 57, business man. History of syphilis 20 years ago. Psychosis began when 54 with change of disposition, gradual loss of business capacity, speech defect, vague persecutory delusions and gradual dementia. Physical examination showed muscle tremors, incoordination, Argyll-Robertson pupils, and hyperactive knee reflexes. Wassermann reaction on the blood negative, on spinal fluid positive, globulin positive, and cells four per cubic millimeter. Death occurred three months after admission and permission for autopsy was refused. However, our diagnosis of general paralysis of the insane is corroborated by similar diagnosis made at the Sheppard and Enoch Pratt Hospital just previous to admission here.

CASE No. 5, HOSPITAL No. 8705.—Patient male, age 52, teamster. No history of syphilis. Psychosis developed at the age of 51 with wandering tendency, rambling incoherent conversation, expansive delusions, inability to accomplish simple tasks and defective orientation. Physical examination showed slightly spastic gait, muscle tremors, Argyll-Robertson pupils, hyperactive knee reflexes, slurring elision of speech, and ironed out facial expression. Two specimens of blood taken with an interval of three months were negative to the Wassermann test. One month later a positive reaction was obtained. The spinal fluid gave a positive Wassermann reaction, positive globulin, and contained five cells per cubic millimeter. The "Goldsol" curve was of the paretic type. Diagnosis paresis.

CASE No. 6, HOSPITAL No. 7597.—Patient male, age 44, fireman. No history of syphilis. Psychosis developed at the age of 39 with diminishing capacity for work, insomnia, poor impressibility of memory, judgment defect, grandiose trend of thought, and lack of insight. A physical examination showed muscle tremors, unequal irregular pupils that reacted poorly to light but well to accommodation, equal but hyperactive knee reflexes, slurring speech and washed out facial expression. Three specimens of blood taken at an interval of one year were all negative to the Wassermann test. Five tests were made on the spinal fluid and all gave a positive W. R.; with globulin positive three times, negative twice; cells varied from 60 to none. Diagnosis paresis.

CASE No. 7, HOSPITAL No. 8187.—Patient male, age 48, salesman. History of syphilis at the age of 20. Psychosis began at the age of 45 with excessive worry over possible results of his early syphilitic infection, which at last became so great as to prevent work and sleep. Made several weak attempts at suicide. Physical examination showed slightly spastic gait, speech defect, pupillary margins irregular and reaction to light impaired and hyperactive knee reflexes. The blood was negative to the Wassermann reaction on six tests. The spinal fluid was at first positive; became negative after Swift-Ellis treatment and then was persistently positive in spite of further treatment. Globulin was positive in the first four tests and negative the last three; cells varied from 24 to none. Patient taken home against advice and has since committed suicide.

CASE No. 8, HOSPITAL No. 8102.—Patient male, age 47, oil-producer. History of syphilis when 19. Psychosis began at the age of 43 with excessive desire to eat and sleep, then a sudden onset of great confusion, restlessness, careless habits, poor memory, and a grandiose trend of thought. Physical examination showed positive Rhomberg, sluggish knee reflexes, irregular pupils that reacted poorly to light, muscle tremors, slight speech defect, and washed out facial expression. Two specimens of blood have given negative Wassermann reactions and the single fluid taken was positive. Globulin positive; cells four per cubic millimeter. Diagnosis paresis.

CASES DIAGNOSED CEREBROSPINAL SYPHILIS.

CASE No. 9, HOSPITAL No. 8571.—Patient male, age 16, school boy. No history of syphilis and both parents have Wassermann negative blood. Normal intelligent child until failing vision began at the age of 12, resulting in a complete optic atrophy a year later. A gradual dulling of all mental faculties began at 13, and resulted in a deep dementia by the time he was 16. A cerebral episode followed by transient loss of speech occurred when he was 15. In walking he took short uncertain steps, moved sideways and tended to travel in circles. Hands were tremulous, he was resistive but not spastic, knee reflexes normal, no pathological reflexes, expression that of an idiot, pupils unequal and failed to react to light or accommodation. W. R. on both blood and fluid positive twice; six weeks

interval. Globulin was negative once and positive once; cells three and six respectively. "Goldsol" curve of the paretic type. The autopsy confirmed the diagnosis of cerebrospinal syphilis.

CASE No. 10, HOSPITAL No. 7854.—Patient male, age 55, traveling salesman. History of syphilis about 25 years ago. Onset at 53 with the sudden development of great weakness of the right leg, hysterical worry and irritability. During his hospital residence he had several convulsions, all confined for the most part to the right side, and following each there was a more marked paralysis of that side. Organic reflexes became impaired and during the last few months a slowly developing weakness of all the muscles was observed. At that time there was a right ankle clonus, Babinsky and Oppenheim; all other deep reflexes much exaggerated on both sides, pupils irregular and reacted poorly and sensation changes were questionable. Failing memory and a suggestion of aphasia were the prominent mental characteristics. Wassermann reactions; blood negative, fluid positive. Globulin positive, cells three per cubic millimeter. Autopsy showed cerebrospinal syphilis with focal lesions.

CASE No. 11, HOSPITAL No. 8149.—Patient male, age 35, boiler maker. History of syphilis at the age of 25. Optic atrophy began at the age of 31 and shortly after that he showed a change of disposition being irritable and subject to periods of very unreasonable anger. No distinct mental disturbance demonstrated while at the hospital. Physical examination showed optic atrophy, sluggish knee reflexes and stiff pupils. Wassermann reaction on the blood positive. Six specimens of the spinal fluid taken over a period of 10 months all gave a positive Wassermann reaction, globulin always positive and the cells varied from three to 100. Diagnosis cerebrospinal syphilis. (The possibility of a later development of taboparesis must be considered in this case. Present symptoms do not justify such a classification.)

CASE No. 12, HOSPITAL No. 8231.—Patient male, age 40, farmer. History of syphilis when 14 years old. When 37 years old he suffered a transient paralysis of both arms. At 39 he had a transient paralysis of the right side of the body. Four months after this sudden paralysis of all four extremities, the muscles of articulation and of deglutition developed. He was unconscious only at the time of the last stroke. This last condition cleared up after a few months except for the muscles of articulation, and during the year that he was under observation he was unable to speak but conveyed ideas clearly by writing. Conduct previous to admission suggested delusions of infidelity and of jealousy, but the presence of these was always questionable. Physical examination showed deviation of the tongue to the left, residuals of a right hemiplegia, paresthesia of the right leg, slight muscle tremors, and paralysis of the laryngeal muscles. Wassermann reactions; blood negative, fluid positive. Globulin test positive, cells five per cubic millimeter. Diagnosis, cerebrospinal syphilis.

CASE No. 13, HOSPITAL No. 8200.—Patient male, age 63, insurance agent. History of syphilis at the age of 39. Beginning at the age of 47 he suffered necrosis of the nasal bones and severe headaches for a period

of two years. When 55 he began to have dizzy spells and transient attacks of monoplegia. Eight months previous to his death the physical disturbances witnessed here began, accompanied by disorientation and clouding of consciousness and several very vague autopsychic delusions. Physical examination showed partial paralysis of both legs, the left being the weaker, and both being a little spastic, impaired vision and hearing, muscle tremors, some difficulty of deglutition, hyperactive left patella reflex, left Babinsky, double Oppenheim, and unequal pupils that reacted well. Wassermann reactions; blood negative, fluid positive. Globulin test positive; cells two per cubic millimeter. Autopsy was refused. Diagnosis cerebrospinal syphilis.

SUMMARY TABLE.

No. Case.	Paresis.						
	Blood.		Spinal Fluid.				
	W. R.		W. R.		Globulin.		Cells.
	+	-	+	-	+	-	
1.....	0	1	7	1	1	7	13 to 0
2.....	0	1	1	0	1	0	40
3.....	7	2	11	0	8	3	70 to 0
4.....	0	1	1	0	1	0	4
5.....	1	2	1	0	1	0	5
6.....	0	3	5	0	3	2	60 to 0
7.....	0	6	6	1	4	3	24 to 0
8.....	0	2	1	0	1	0	4

No. Case.	Cerebrospinal Syphilis.						
	Blood.		Spinal Fluid.				
	W. R.		W. R.		Globulin.		Cells.
			+	-	+	-	
9.....	2	0	2	0	1	1	3 to 6
10.....	0	1	1	0	1	0	3
11.....	1	0	6	0	6	0	3 to 100
12.....	0	1	1	0	1	0	5
13.....	0	1	1	0	1	0	2

Figures represent the number of positive or negative reactions in the individual cases.

Summary.—In the series of routine cases presented here:

1. A positive W. R. in the blood seems to be the rule, but even repeated negative findings do not exclude a diagnosis of paresis.
2. The blood W. R. may or may not be positive in cerebrospinal syphilis.
3. A positive W. R. was found in the spinal fluids of all paretics and cerebrospinal syphilitics.
4. The globulin reaction was very inconstant in both conditions and of no aid in the differential diagnosis.
5. The cell count varied greatly in both conditions, but was as great in one as in the other.
6. The five cases of cerebrospinal syphilis with uniformly positive W. R. in the spinal fluids, two positive and three negative bloods, show clearly the difficulty in diagnosis by laboratory methods alone.
7. Cases three and five demonstrate the necessity of making a series of tests whenever possible.
8. Experience with these and many other cases inclines the authors to believe that all the bloods here reported as negative would have given positive reactions to the Wassermann test if there had been an opportunity to make a series of tests.
9. Satisfactory diagnosis can only be made when the clinical and laboratory findings are considered together.

REFERENCES.

1. American Journal of Insanity, Vol. 65, p. 662.
2. American Journal of Insanity, Vol. 69, p. 243.
3. Journal of Medical Research, Vol. 30, No. 3, p. 377.