

Vaccination efficiently performed silences opposition.

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CORRELATIONS OF CEREBRO-SPINAL FLUID EXAMINATIONS WITH PSYCHIATRIC DIAGNOSES. A STUDY OF 140 CASES.*

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THE scarcity of actual correlations between findings in the cerebrospinal fluid and psychiatric diagnoses in any considerable series of cases makes of value a review of the results in a large hospital for the insane. The object of the present study has been to discover of how much value examinations of the cerebrospinal fluid have been in changing, confirming or making more accurate the psychiatric diagnoses. The focal points of interest in this connection are, of course, the diagnosis of paresis and of cerebral syphilis. It may be said in a general way that this review has shown that paresis is not actually as frequent as would appear from purely clinical examination, and that the cases which are most likely to be mistaken for it are Korsakow's psychosis, cerebral arteriosclerosis and cerebral syphilis.

The method† adopted in this hospital is to have a Wassermann test made on the serum of each new patient unless this has been recently done in another institution. If the result is positive, and also in negative cases in which the symptoms or signs are suggestive, the cerebro-

spinal fluid is examined for the Wassermann reaction, cytology and globulin content. Similar tests are being carried out also on old patients as rapidly as possible. The Wassermann reactions are done at the laboratory of serum diagnosis of the Harvard Medical School. The remainder of the examination, except the differential count, may be done by a non-medical laboratory assistant, who is familiar with blood counting and elementary chemistry.¹

Statistics. The period chosen for study was the year ending Jan. 1, 1914. During this time 626 Wassermann reactions have been done on the sera of 618 patients, 445 of whom were admitted in 1913, and 173 before that time. The 1913 admissions form an unselected group from which may be estimated the frequency of syphilis in patients admitted to this hospital. The results are:

Wassermann reaction in the serum positive in 80 cases (18%).

Wassermann reaction in the serum negative in 362 cases (81.3%).

Wassermann reaction in the serum doubtful in 3 cases (0.7%).

This percentage of positive sera is lower than that of Paine,² who in his study of 200 consecutive admissions to the Danvers State Hospital found 24.5% positive.

During the year ending Jan. 1, 1914, 142 cerebro-spinal fluids from 140 patients have been examined for the Wassermann reaction. Of the 76 specimens from 1913 admissions, 33 (43.4%) gave a positive, 43 (56.6%) a negative result.

CLASSIFICATION.

We have used as a basis of our grouping of the fluids for study, the diagnosis given by the physician on the card accompanying the specimen to the laboratory, combined with the serological and cytological findings in the fluid. It must be emphasized in the beginning that in many instances this clinical diagnosis represents not the final, but the provisional diagnosis after the routine physical and mental examination, and is made with the reservation that it may be changed by the serological and cytological evidence.

follows: to 0.2 cc. of cerebro-spinal fluid, 0.5 cc. of a 10 per cent. solution of butyric acid in normal salt solution is added, and the mixture heated to boiling. One-half a cc. of normal sodium hydroxide solution is added, and the tube boiled slightly. A flocculent precipitate within 15 minutes indicates a positive result.

For the cell count in the fresh fluid, 0.1 cc. of 3 per cent. acetic acid and 1 cc. of cerebro-spinal fluid (well shaken) are mixed in a white blood counter, and ten fields are counted.

The sediment is prepared for differential counting by the Alzheimer method, *i.e.* by adding to 3 or 4 cc. of cerebro-spinal fluid twice its volume of 95 per cent. alcohol, centrifuging for one hour at high speed, and hardening the precipitate in absolute alcohol, followed by absolute alcohol and ether. The coagulum is removed from the centrifuge tube with a pointed glass rod; embedded in celloidin; cut in sections 7 m. thick, and stained with pyronin-methyl-green. In fluids showing a high or moderate pleocytosis 200 cells were counted. When cells were present in normal or slightly increased numbers, several sections (5 to 8) were gone over carefully and the actual number of each variety of cell present was stated.

* Worcester State Hospital Contribution No. 20 (1914. 1).

† METHOD.—The following is the method adopted for the Wassermann reaction: "Three antigens differing in fixing power are used for each specimen. Two are from human hearts and are reinforced with cholesterol; the third is the alcoholic extract from a fetal syphilitic liver. The complement, which is ten per cent. guinea-pigs' serum, is titrated daily to determine the unit; two units are used in the test. The amboceptor is titrated against .5 cc. of 10 per cent. guinea-pigs' complement in order to determine the amboceptor unit. Two units are used in the test. The amboceptor value is re-determined before each test. Washed sheep's corpuscles, are made up with normal salt solution to 5 per cent. suspension. Five-tenths of a cubic centimeter is used."

"The following controls are used for each test: a strongly positive syphilitic serum; a weakly positive serum; a negative serum, and tubes containing double the amount of each antigen."

"All doubtful cases are repeated at the next test, and if there is sufficient serum, varying amounts of antigen and serum are used, so that the resulting test rarely gives a doubtful result."

The Noguchi test for globulin was used, and was performed as

The following classification was adopted:—

1. Cases diagnosed clinically as paresis, with which the findings in the fluid were on the whole in accord; 47 cases.

2. Cases diagnosed as paresis, in which the spinal fluid was negative or doubtful; 13 cases.

3. Cases in which the fluid was sent in to the laboratory with the diagnosis "Paresis?"; 20 cases.

4. Cases of organic dementia, including cerebral syphilis; 15 cases.

5. Alcoholic group, including both the acute and chronic forms; 10 cases.

6. Negative fluids from a variety of conditions, including manic-depressive insanity, dementia precox, imbecility, etc. These will not be further considered here.

It is obvious that in this group there is considerable latitude of judgment given on both the clinical and the laboratory sides, but at least it brings out the difficulties of diagnosis and the type of case in which the examination of the cerebro-spinal fluid is of particular value.

Group 1. In this group of 47 cases the Wassermann reaction on the serum was positive in 41 cases, negative in 4, and not recorded in 2 cases. The cerebro-spinal fluid was positive in 36 cases, negative in 9, and not recorded in 2 cases. The serum and fluid were both positive in 36 cases, the serum positive and fluid negative in 5 cases, the serum negative (tested twice) and fluid positive in one case; both serum and fluid negative in 3 cases, and one or the other not recorded in 2 cases.

All these fluids except one, however, showed a pleocytosis, and all but two contained plasma cells. All gave positive ammonium sulphate or Noguchi reactions, usually in high dilutions.

The Wassermann reactions, with the one exception mentioned have not been repeated in cases giving negative results. We should not consider that a single negative report on the fluid where it is impracticable to use "auswertung" methods would weigh decisively against the diagnosis of paresis, if the cytology and clinical picture were typical. Cases showing a positive reaction in the serum and a negative one in the fluid, with a positive cytology, suggest, of course, cerebral syphilis in contradistinction to paresis, and cases in which the serum and fluid are both negative can be put in the paresis group only if the clinical and cytological evidence is very strong.

Schoenhals⁴ has recently reported four cases of clinically typical paresis, in which serum and fluid gave repeated negative reactions, but in which the globulin test and the cytology were positive. In three of the cases the diagnosis of paresis was verified by autopsy. All the cases were of the slowly progressing form.

Two of the cases in this series having negative reactions in both serum and fluid are clinically advanced cases of the dementing form of paresis of at least one and a half and two and a half

years' duration, respectively. One shows Argyll-Robertson pupils, tremors and practically normal knee kicks; the other slurring speech, rigid pupils, absent knee kicks, incoordination and a positive Romberg sign. The third is apparently an early case of the expansive form, with unequal pupils, reacting sluggishly to light, exaggerated and unequal knee kicks, unsteadiness and tremors.

Of the cases with the Wassermann positive in the serum and negative in the cerebro-spinal fluid, it may be said in a general way that the clinical picture and physical signs are more in accordance with paresis than with cerebral syphilis. In two cases the infection was respectively at least twenty and twenty-three years before the beginning of the psychosis; in the other three cases, the date of infection is unknown. The onset was gradual in all cases. Four of the patients are in an advanced stage of dementia, while the fifth is apparently an early case of the expansive form. Two of the patients have Argyll-Robertson pupils, two contracted pupils, inactive to light, and reacting only slightly to accommodation; the fourth has active pupils. One of the cases is of eleven years' duration.

Group 2. In the second group, those cases diagnosed clinically as paresis, but with doubtful or negative findings in the cerebro-spinal fluid, are two cases typical clinically of the expansive form of paresis. In one the fluid was taken on the day of death, in the other a week before. The sera were both positive, one fluid positive, the other negative. The globulin reactions were slight, the cell counts within normal limits and the sediments showed small numbers of lymphocytes and endothelial cells, with, in one case, possible plasma cells. Unfortunately, no autopsies were obtained, but it seems probable that the terminal stage of the disease may account for the indefinite findings.

In this group is also one other case with anomalous findings: a patient with the clinical symptoms of the dementing form of paresis, with pupils reacting sluggishly to light, exaggerated knee jerks, unequal facial innervation, and slight Romberg sign. The Wassermann reaction was negative in the serum, positive in the cerebro-spinal fluid. The examination of the first specimen of fluid showed a slight Noguchi reaction, a slight cell increase consisting of lymphocytes with a few doubtful plasma cells. The second specimen, taken a month later, gave negative ammonium sulphate and Noguchi reactions, a normal cell count and only a few lymphocytes in the sediment.

Another patient in this series has the following history: 58 years old, a painter for 25 years. In the Worcester State Hospital four and a half years. Has had both lues and numerous attacks of lead colic and has used alcohol in moderation. Six months before admission patient lost interest, became reticent, and irritable, and had attacks of dizziness. On admission he was quiet, euphoric, with delusions

of persecution and reference. He was imperfectly oriented for time and place; had but slight grasp on his surroundings and no insight. Memory was fair; speech somewhat slurring, pupils active, gait unsteady, knee jerks exaggerated, suggestive Romberg's sign. The patient is in a stationary condition, and although quite irritable, is able to work regularly. The Wassermann reaction was negative in the serum, doubtful in the cerebro-spinal fluid. The latter gave negative globulin tests, but a slight lymphocytosis. It is possible that this may be a case of lead encephalitis, although there is no very definite evidence to support this view.

The revised diagnoses in the other cases of this series are: Korsakow's psychosis, 3 cases; acute alcoholic delirium (terminating fatally, no autopsy), 1 case; dementia precox, 3 cases; unclassified depression, 1 case.

On examination of the histories of the patients who proved not to be paretics, the reason for the diagnosis of general paralysis is in most cases obvious. All the cases presented more or less suggestive physical signs, ranging from pupillary inequality, tremors or changes in the reflexes to sluggish reaction to light, speech defect, and in some of the alcoholic cases ataxia. In four cases also the Wassermann reaction in the serum was positive, in two others there was a history of syphilis, while in four syphilis was denied and the Wassermann reaction in the serum was negative. Another fact standing out prominently in this group is alcoholism, which was present in all but one of the cases.

Group 3, in which the fluids were sent to the laboratory with "question of general paralysis," comprises 20 cases. The diagnosis was confirmed in five cases by positive Wassermann reactions in serum and fluid and typical cytology in the latter.

One of these, a man of 61 years, had previously been diagnosed an early senile dementia. The diagnosis of paresis in this case has been substantiated by autopsy. Another patient, a woman, 54 years old, was admitted after a suicidal attempt, showing depression with psychomotor retardation, but without physical signs. The first diagnosis was manic-depressive, or a depression of arteriosclerotic origin. The patient is now dementing, is confused and excitable, and definite signs have appeared.

One case of clinical paresis examined a week before death showed conditions somewhat similar to the terminal cases mentioned in Group 2. The serum gave a negative reaction, the fluid a suggestion of a positive. The globulin was considerably increased, the cell count normal, and the sediment contained small numbers of lymphocytes and endothelial cells. The revised diagnoses in this group are: Alcoholic hallucinosis, 2 cases; acute alcoholic delirium, 1 case; alcoholic deterioration, 1 case; dementia precox, 6; manic-depressive with deterioration, 1 case; manic phase of manic-depressive insanity, 1 case.

A study of the histories of these cases brings

out the frequency of the same three factors noted in the previous group,—physical signs, syphilis and alcohol. Ten patients in addition to those in whom the diagnosis of paresis was confirmed, had positive Wassermann reactions in the serum, one other gave a history of syphilis, one had signs of the disease, two denied lues and had negative Wassermann reactions, and in one case no clinical history was obtained. Nine patients, exclusive of the paretics, had a history of alcoholism.

Group 4, that of the organic dementias, contains 15 cases. The examination of the blood and cerebro-spinal fluid has helped considerably to differentiate the etiology of these cases. In seven the Wassermann reaction was positive in the serum, and negative in the cerebro-spinal fluid. Two of these showed negative globulin reactions and negative cytology, the other five a positive globulin reaction, lymphocytosis, with, in three cases, the addition of plasma cells. One of these patients, diagnosed paresis during life, was found at autopsy to have cerebral gummata. In one case in which the serum was not recorded the fluid gave a negative Wassermann reaction, but a positive globulin test and a lymphocytosis. One case presented a negative Wassermann reaction in the blood and a positive in the fluid, with increased globulin content and a lymphocytosis. In five cases the serum and fluid were entirely negative. In five of this group, therefore, in addition to the autopsied case, it seems permissible to assume a syphilitic etiology for the trouble.

Group 5. Ten fluids were sent in from patients with the diagnosis of various forms of alcoholic psychoses: acute alcoholic hallucinosis, 5 cases; chronic alcoholic hallucinosis, 1 case; alcoholic deterioration, 2 cases; Korsakow's syndrome and alcoholic traumatic, each 1 case. One of these cases had a positive Wassermann reaction in the serum, and a negative one in the fluid, but an increase of globulin and a lymphocytosis. One other had similar findings, with the exception that the Wassermann reaction in the fluid is not recorded. Four patients had positive Wassermann reactions in the serum, but cerebro-spinal fluids negative serologically and cytologically. One case with a negative reaction in the serum but in whom the Wassermann reaction in the fluid was not recorded, had a slight increase in globulin, but negative cytology. One case gave negative reactions to all the tests, and one an isolated positive Wassermann in the spinal fluid. One patient on whom the diagnosis of alcoholic hallucinosis was made, was found to have a positive Wassermann reaction in serum and cerebro-spinal fluid, an increase of globulin, and a pleocytosis, with the presence of plasma cells. It is impossible to exclude cerebral syphilis in the alcoholic cases who show a positive Wassermann reaction in the serum, a lymphocytosis and globulin reaction in the cerebro-spinal fluid, and doubtful physical signs.

DISCUSSION.

In reviewing these groups, it is found that among 80 patients in whom the diagnosis of paresis was made definitely or in whom a suspicion of it was entertained, in 57 at the most (71%) the diagnosis appears to be confirmed after examination of the serum and cerebro-spinal fluid. In the 60 cases in which the diagnosis was made definitely, it seems to be substantiated by serological and cytological evidence in 50 cases, or 83%.

On the other hand, three cases of paresis have been discovered by the routine examination of the serum and cerebro-spinal fluid in patients diagnosed on admission as senile dementia, arteriosclerotic depression and alcoholic hallucinosis.

The groups into which the non-paretic cases fall are: the alcoholic, 10; the dementia precox, 9; the manic-depressive, 2; unclassified depression and undiagnosed, 1 each. The revised diagnosis in all the cases, except possibly the Korsakows, would doubtless have been attained by clinical observation alone in the course of time, but for rapid elimination of the suspicion of paresis, the serological and cytological examination of the cerebro-spinal fluid is essential. It is also a common experience in large hospitals that there are on the chronic wards certain demented patients who are supposed to be long-standing cases of paresis, the diagnosis having been made on their admission in pre-Wassermann days, and never challenged. When their sera and fluids are examined, however, the results in a certain proportion of cases are found not to be in accord with the diagnoses and the cases appear on closer inspection to be cerebral arteriosclerosis or syphilis, or Korsakow's psychosis.

Correlations of clinical and autopsy findings from the Danvers⁵ and the Worcester State Hospitals⁶ in pre-Wassermann days have shown that there is a positive error of about 15% in the clinical diagnosis of paresis. The study of clinical diagnoses before and after examination of the serum and cerebro-spinal fluid goes to prove the same point, *i.e.* that paresis is actually not as frequent as it appears to be from purely clinical observation.

Since Wassermann tests and cerebro-spinal fluid examinations have been commenced, however, the tendency in this institution at least, has been toward more reserve in the diagnosis of paresis, and more care has been exercised in making a differential diagnosis, particularly from cerebral syphilis and arteriosclerosis.

CONCLUSIONS.

Our conclusions may be summarized as follows:

1. Examination of the serum and cerebro-spinal fluid leads to a reduction in the number of cases diagnosed as general paralysis.

2. The cases which have been found most difficult to differentiate from paresis without examination of the serum and cerebro-spinal fluid are cerebral syphilis and arteriosclerosis and Korsakow's psychosis. In regard to cerebral syphilis, however, it must be said that although the findings in the serum and cerebro-spinal fluid are supposed to be sufficiently characteristic to permit a differential diagnosis from paresis, in the individual case they frequently leave one in doubt.

3. In a large insane hospital the routine examination of the serum and cerebro-spinal fluid finds, perhaps, its most immediate value in the rapid confirmation or elimination of the suspicion of paresis in new patients and in revision of the diagnoses of certain patients admitted in pre-Wassermann days.

Thanks are due to the staff for help in collecting the clinical data.

REFERENCES.

- ¹ The cell counts and globulin reactions in this series have been done by Miss Marion Slater Stone, A.B.
² BOSTON MEDICAL AND SURGICAL JOURNAL, Vol. clxviii, No. 14, April 3, 1913.
³ The amount of cerebro-spinal fluid used for the Wassermann reaction in these cases was 0.5 cc.
⁴ Schoenhals: *Monatsschr. f. Psychiatrie u. Neurologie*, Vol. xxxiv, No. 48, p. 280, Sept., 1913.
⁵ Southard: *Journal of Nervous and Mental Diseases*, Vol. xxxvii, No. 1, Jan., 1910.
⁶ Orton: To be published soon.

TWO CASES OF LUNG ABSCESS CURED BY OPERATION.

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These two cases are reported because in each an abscess of the lung followed immediately after taking ether. One patient had been operated on for a deviated septum and the other had had several teeth extracted. It seems probable that both these cases were due to aspiration of some infective substance.

Both cases are perfectly well at the present time. The first case was operated on a year and three months ago and the second four months ago.

I criticize my technic in the first case at the present time because the operation was done at one sitting. The lung seemed to be adherent to the lower half of the pleura that was exposed in the field of operation, but although I stitched the lung to the pleura before opening into the abscess, yet this patient developed an empyema two weeks after the operation, which I feel was due to leakage of septic material into the pleural cavity. This necessitated a second operation, from which the patient made a speedy recovery.

I think the technic I used in the second case a much safer one. In this case at the first opera-