

CHICAGO NEUROLOGICAL SOCIETY

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The President, DR. L. HARRISON METTLER, in the Chair

REPORT OF A CASE OF INFLUENZAL MENINGITIS

By David J. Davis, M.D.

The interesting features of the case may be summarized as follows: A purulent cerebro-spinal meningitis occurred in an infant four days after birth and also very probably in his twin brother. Clinical signs of meningitis were not prominent. Death occurred after four days and at necropsy the influenza bacillus was found in pure growth in the meningeal exudate and peritoneal cavity, but not in the heart's blood. The atria of infection usually inspected in these cases were normal, namely, the tympanic cavities, nasal cavities, throat and lungs. An acute enteritis existed, which may have been the origin of infection. There was no evidence of influenza infection in the mother or other members of the family.

The literature has been thoroughly reviewed recently. Adams¹ in 1907 tabulates 21 cases in which the influenza bacillus was isolated from the meningeal exudate in pure culture. Cohoe² this year finds 25 cases, including one of his own, and gives an analysis of the important features.

Dr. L. Harrison Mettler said that Dr. Davis stated that this form of meningitis seems to be characteristic of children, and yet general influenza without meningitis seems to be most common in adults. Is there any comparison between the number of cases of influenzal meningitis in children and influenza without meningitis in children? We usually think that meningitis is particularly prone to complicate the infections characteristic of childhood. There may be a parallelism. However, influenza occurs rarely in children, whereas meningitis is comparatively frequent. In the adult the opposite is true.

Dr. Peter Bassoe requested that Dr. Davis say something about the proof of the influenza bacillus being the cause of influenza, as he has done much work along this line for several years.

Dr. Davis said, Pfeiffer, in 1892, announced the discovery of the influenza bacillus in epidemic influenza. Following this announcement much work was done by the Germans to substantiate this statement. However, for several years it was impossible to find this organism in a large proportion of cases of epidemic influenza, so that many workers doubted the specificity of Pfeiffer's bacillus as the cause of influenza. The French never believed in this specificity. It was also found that Pfeiffer's bacillus could be isolated in many cases of whooping-cough, measles and scarlet fever; in fact, it frequently was the predominating organism in the sputum. It has never been found in the blood, however, except in two or three cases of endocarditis. A study of epidemics of influenza in which the cases were typical disclosed a variety of organisms, such as the micrococcus catarrhalis, the streptococcus, pneumococcus, etc. Occasionally, the influenza bacillus is found. Dr. Davis had occasion to examine a number of cases that occurred during the epidemics of 1905 and 1908. The cases were typical clinically, and yet in 1905 Dr. Davis

¹ Adams, Archives of Pediatrics, 1907, 24, p. 721.

² Cohoe, American Jour. of the Med. Sciences, 1909, 137, p. 74.

found the bacillus in only about 15 or 18 per cent. of cases examined, and last year found it in about 20 per cent. of the cases. As a rule the streptococcus is present in large numbers, so that there can be no question that the cases ordinarily called grippe are not due to Pfeiffer's bacillus. Pfeiffer's bacillus is also found in normal throats, so that the question arises whether it is of any significance as an etiologic factor. There can be no question about the pathogenicity of the germ; the case Dr. Davis reported is an instance in point. He has taken the organisms isolated from the sputum of cases of pneumonia and whooping-cough, transplanted them on the tonsils of normal persons, and obtained constitutional symptoms, so that the organism is not a saprophyte in all conditions.

Influenza is not common in children and there is absolutely no relation between the occurrence of influenzal meningitis and epidemics of grippe.

THE WASSERMAN TEST, WITH SPECIAL REFERENCE TO ITS APPLICATION IN NERVOUS AND MENTAL DISEASES

By F. G. Harris, M.D. (By invitation)

The Wasserman reaction is an application of the principle discovered by Bordet and Gengou, *i. e.*, that a suspension of bacteria when mixed with the inactivated serum of an animal previously made immune to that bacterium would bind complement. This reaction was rapidly taken up by dermatologists and syphilographers, and as a consequence our ideas of the various phases of syphilis have been markedly altered.

The five factors that we deal with are (1) antigen, (2) antibody, (3) complement, (4) hemolytic amboceptor, (5) red blood cells.

The technique is complicated and requires careful work. All sera must be tested against normal and syphilitic sera. In the absence of our ability to grow the spirochete an alcoholic extract of a liver of a syphilitic infant is used.

In spite of the fact that the hypothesis on which the serum diagnosis was founded has been shown to be false, it would be wrong to assume that that fact lessens the value of the reaction.

A positive reaction is not found in any other disease except trypanosomiasis, durine, frambosia tropica, some cases of leprosy and possibly some cases of scarlet fever.

The following reports show the immense value of the Wasserman reaction in neurology, especially in regard to paresis:

Wassermann and Plaut (early work) ..	54 cases	90.7% positive.
Morgenroth and Stertz	8 cases	100 % positive.
Marie and Levaditi	30 cases	93.3% positive.
Ravault and Petit	72 cases	93 % positive.
Stertz	45 cases	97.9% positive.
Edel	22 cases	95.5% positive.
Meier	39 cases	100 % positive.
Plaut	44 cases	100 % positive.
Lesser	37 cases	100 % positive.
	351 cases	97.8% positive.

Of 1,188 cases of paresis collected from the literature 96.5 per cent. showed a positive reaction.

There seems to be little difference in regard to the duration of the disease, as early cases show the reaction as well as advanced ones. The reaction is especially useful in differentiating paresis from mania, imbecility, senile dementia, Korsakoff's psychosis, neurasthenia, etc.

The results in tabes are not so striking.

Citron reports 15 cases.....	80 % positive.
Fleischman reports 16 cases.....	81 % positive.
Eichelberger reports 49 cases.....	65 % positive.
Liderman reports 41 cases.....	75.6% positive.

Of 280 cases of tabes collected from the literature 72.6 per cent. showed a positive reaction in the blood or spinal fluid.

The striking contrast between the results in paresis and tabes is accounted for as follows, namely, that paresis is not considered para-syphilitic, but as a manifestation of active syphilis (a meningo-encephalitis), and that tabes is looked upon as a chronic syphilitic meningitis of the cord with a subsequent degeneration of the posterior tracts, the more prolonged course of tabes allowing time for the syphilis to be cured.

Of 40 cases of cerebro-spinal syphilis 52.5 per cent. showed a positive reaction. In most of these cases the spinal fluid was tested, which is usually negative, whereas the blood is usually positive.

A positive reaction does not occur in non-syphilitic conditions. Of 229 cases examined all showed a negative reaction.

Numerous cases giving a positive reaction have changed to a negative reaction under treatment. Are we predicting too much when we say that the future treatment of syphilis will be a biologic treatment, *i. e.*, controlling the treatment from time to time by a Wasserman reaction?

The author has examined 27 cases of tabes, 19 gave a positive reaction, *i. e.*, 70.3 per cent.

He has also examined

1 case of spastic paraplegia	positive.
1 case of cerebro-spinal syphilis	positive.
1 case of paresis	positive.
1 case of syphilitic meningitis	positive.
1 case of syphilitic hemiplegia	positive.
1 case of arteriosclerotic softening	negative.
1 case of diabetic pseudo-tabes	negative.

Dr. Hugh T. Patrick inquired whether in cases of paresis and tabes with a positive reaction the administration of mercury produces a negative reaction. That is very interesting, because of the fact that in paresis the administration of mercury not only fails to produce a cure, but fails to arrest the course of the disease, although it sometimes appears to have a favorable influence on it. The same thing applies to tabes, although many of these cases have remissions, so that the conclusion as to the effect of any therapeutic measure can never be as definite as in the case of paresis. However, there is no very strong evidence to show that the administration of mercury definitely arrests the course of tabes any more than it does the course of paresis.

The case of arteriosclerotic softening which Dr. Harris examined was exceedingly puzzling from the physical as well as the mental standpoint, and after Dr. Harris's examination Dr. Patrick finally concluded that the case was probably one of paresis. Dr. Harris reported a negative reaction.

The patient died and the post-mortem findings of advanced atheroma with two large areas of softening in the brain, evidently of arteriosclerotic origin, sustained the conclusions drawn from the Wasserman test.

Dr. R. C. Hamill said the cases which Dr. Harris got from the infirmary at Dunning were interesting in that the negative ones had a shorter duration of tabes than the positive ones. The latter had existed about fourteen years, and the former seven to four years. The time elapsed since infection with syphilis in the negative cases gave an average of 25.2 and in the positive ones 20.6 years. One of the negative cases had chancre twelve years before and tabes for only four years, but at a rapidly progressing course. The ataxia is worse now than it was a year ago and he has constant severe pains, bladder crises, has lost control of his urine and is getting worse rapidly. On the other hand, some of the positive cases are of very long standing, some as long as twenty-five years, with the tabes of sixteen years' duration.

Dr. Peter Bassoe mentioned one case in which the Wasserman test was exceedingly valuable; in fact, it was the only means of making a correct diagnosis. A child of ten years had peculiar mental symptoms and a peculiar form of spastic paralysis. None of the ordinary signs of congenital syphilis were present. Dr. Harris obtained a positive reaction. At necropsy the brain revealed a general fibrous leptomeningitis which could hardly be anything but syphilitic. Dr. Bassoe cut out some pieces and stained for the spirochete with negative results. In regard to the clinical value of the test one thing ought to be emphasized. We are not satisfied to know that the patient has had syphilis, but we must be able to determine that the nervous symptoms present are due to syphilis. That problem comes up time and time again. At the Cook County Hospital they repeatedly heard patients give a history of all varieties of venereal infection, but they usually also are alcoholics and it is then difficult to interpret the symptoms presented. There may be a question whether the case is one of genuine tabes or alcoholic pseudo-tabes. If examination of the cerebro-spinal fluid gives a positive Wasserman test, and if this always means active syphilis of the nervous system, it helps a great deal, and if there also is lymphocytosis and a positive globulin test is obtained, Dr. Bassoe believes that the evidence is quite strong that the case is one of active syphilis of the nervous system. He would like to have Dr. Harris say whether he has found any exceptions to the rule that a positive test with the cerebro-spinal fluid means syphilis of the nervous system. A recent paper by Nonne disclosed some peculiar discrepancies. There were several positive tests in cases that did not appear to be syphilitic, such as multiple sclerosis and epilepsy, which made Nonne rather cautious in accepting the reliability of the test. Pappenheim in a recent paper claims that the Wasserman test is not a specific reaction for syphilis, but is due to the presence in the fluids examined of products of cell destruction, and that the reason we so frequently get the positive test in syphilis is that this disease is attended by destructive processes which liberate large amounts of globulin, thus explaining the positive Wasserman and globulin tests.

Dr. D'Orsay Hecht asked Dr. Harris what he thinks of the Noguchi modification of the Wasserman test and its value.

Dr. Harris said in regard to Dr. Patrick's question, as to the effect of mercurial treatment on the reaction, the bulk of the work done with this test has been in clinics, where only advanced cases are seen. How-

ever, if treatment is of any value in nervous diseases showing a positive Wasserman reaction, it is in the early cases. He has not seen any reference in the literature to a change from a positive to a negative reaction in nervous diseases. One thing learned from the Wasserman test is that we have not been treating syphilis properly. We do not treat these cases enough, and it is only by giving enough treatment that we can expect to change the positive into a negative reaction. Of course a positive Wasserman is of value only in that it shows that there is syphilis somewhere in the body. It does not indicate what organ is affected. If an examination of the cerebro-spinal fluid shows a positive reaction then the lesion is somewhere in the nervous system. It is in the alcoholic cases that Nonne found the reaction, but it is quite likely that these patients have a syphilitic focus somewhere in the body, and that the nervousness is due to the alcohol. Nonne's statistics come from Hamburg and should be regarded with some skepticism. He cites cases of multiple sclerosis and epilepsy as giving a positive reaction, but the tests were made by Eichelberg and Much. They report 40 per cent. of cases of scarlet fever as showing a positive Wasserman, but other observers were unable to substantiate these findings.

One worker in Copenhagen found that quite a number of cases of scarlet fever gave a positive reaction, but he was able to prove that this result was due to a change in the antigen. Working with aqueous extracts, which change from time to time, such results are produced; alcoholic extracts are more stable.

As to Noguchi's work, Dr. Harris understands he works with dried blood and human complement. The crux of the whole thing is this: If we add a small amount of antigen and of antibodies to an excessive amount of complement the reaction is negative. The antibody is an unknown factor, therefore results are not so reliable as where we are working with a known factor. Therefore, use less complement than is necessary to satisfy these two factors, so that none will be left over, to produce a negative reaction. Why a guinea-pig heart should act as antigen is not known, except that it contains a lipid, which has the ability to unite with something in the syphilitic blood and bind the complement. This does not occur in as large a percentage of cases as when syphilitic liver antigen is used. It is also a fact that those who have used guinea-pig heart fail to get a positive reaction where it has been obtained when liver antigen was used. That complicates the compilation of statistics and makes such statistics as we have of less value. The only reliable antigen is extract of syphilitic liver.

As to Pappenheim's idea that the globulin was due to tissue destruction, it is well known that there is much tissue destruction in every case of infectious disease, yet in none of them do we get the Wasserman reaction. It has never been recorded in pneumonia, tuberculosis and other severe destructive processes, such as acute yellow atrophy or hepatic cirrhosis. Nonne reported a case of multiple sclerosis and one of tumor which gave a positive reaction.