

## An Analysis of the Results of the Wassermann Reactions Obtained from 2,000 Consecutive Pregnant Women.

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THE difficulty of the clinical diagnosis of syphilis in the pregnant woman is well known to all workers at antenatal clinics. The frequent absence of a history of infection or of clinical manifestations of the disease in the pregnant syphilitic woman, which was first recorded by Colles nearly one hundred years ago, is now a well-recognized fact. The occurrence of these clinically negative cases calls for the use of an aid in the diagnosis, namely the Wassermann reaction. The following report is the result of an investigation which was undertaken in order to estimate the value of the routine use of the Wassermann reaction at antenatal clinics.

F. J. Browne<sup>1</sup> investigated the histories of 100 women suffering from syphilis who had passed through the indoor department of the Venereal Diseases Clinic of the Edinburgh Royal Maternity Hospital, and obtained a history of infection or of primary or secondary manifestations in only 2 per cent. of multiparæ, while he obtained signs of syphilis in 75 per cent. of syphilitic primigravidæ. He noted, further that when signs of syphilis were absent in primigravidæ, the patients were usually elderly with old-standing infection. From this investigation also, Browne suggested that pregnancy has little or no influence in modifying the Wassermann reaction.

Boas, Gammeltoft and Siecke<sup>2</sup> investigated the Wassermann reaction in 2,200 pregnant women and obtained a positive result in 6.7 per cent. of the cases. The test was repeated one or two years later with practically similar findings, confirming that the positive responses had not been due to pregnancy and childbirth. They concluded that the Wassermann reaction was as trustworthy during these conditions as at other times.

It is well known that syphilis takes a high place among the causes of still-birth and neo-natal death. F. J. Browne<sup>3</sup> found 17.5 per cent. of cases, in a series of 400 examined, to be due either to certain or to possible syphilis. Eardley Holland,<sup>4</sup> in a series of 300 cases, found syphilis to be the cause—either certain

or possible, in 15.3 per cent. Further it is known that syphilis is the cause of death in a high percentage of children under one year. E. T. Burke<sup>5</sup> gives 30,000 as the figure of annual stillbirths and deaths from syphilis under one year. Syphilis is one of the causes of still-birth which can be prevented by treatment if detected sufficiently early in the pregnancy. Ballantyne<sup>6</sup> quotes the figures for the Edinburgh Royal Maternity Hospital in which syphilis was the cause of death among foetuses and newborn infants in 606 per 1,000 among expectant mothers suffering from venereal diseases and with neither supervision nor anti-syphilitic treatment in their pregnancies and 50.7 per 1,000 among expectant mothers suffering from venereal diseases but with ante-natal supervision and treatment during their pregnancies.

The knowledge of these facts together with a desire to ascertain how many cases of syphilis had been detected by the routine use of the Wassermann test led to the present investigation as it was thought that this information would be, at least, of interest to workers at ante-natal clinics.

This report deals with the results of the Wassermann reaction obtained from two thousand consecutive pregnant women, who attended the Ante-Natal Clinic at the Edinburgh Royal Maternity Hospital during the period February, 1925 to August, 1926.

The blood for the Wassermann test was taken at the patient's first visit to the clinic, when the ordinary routine clinical examination was carried out. After a positive reaction was reported an attempt was made to elicit a history of infection or of primary and secondary manifestations, and a more thorough examination was made for specific manifestations. Anti-syphilitic treatment was given at the clinic and the patient observed during the whole of her pregnancy. The majority of these women were confined in the Venereal Diseases Department of the Royal Maternity Hospital, and the Wassermann test was carried out on blood of the umbilical cord, on the puerperal blood and, occasionally, on the blood of the infant. After confinement, the patients were transferred to other venereal diseases treatment centres. This inevitably meant that a few cases ceased attending for treatment, so one was able to trace only a little over 30 per cent. of the total syphilitic patients.

The actual Wassermann test was done at the Royal Infirmary, Edinburgh, where a modification of Harrison's technique is used.

A Wassermann report other than negative was obtained in 130 out of the two thousand patients examined. For the purposes of a closer investigation the cases to be analysed have been subdivided into six groups.

Group I. Women with a triple positive Wassermann reaction either at the first or subsequent test, and those who were sent from a venereal diseases centre with a history of a triple positive Wassermann reaction. Number of cases=73 or 3.6 per cent.

Group II. Women whose highest Wassermann reaction was reported as moderately strong positive. Number of cases=6 or 0.3 per cent.

Group III. Women whose highest Wassermann reaction was reported as weak positive. Number of cases=28 or 1.4 per cent.

Group IV. Women whose Wassermann reaction was reported as doubtful. Number of cases=17 or 0.8 per cent.

Group V. Women whose serum was anticomplementary. Number of cases=6 or 0.3 per cent.

Group VI. Women with a negative Wassermann reaction, but who were considered to be syphilitic. Number of cases=15 or 0.7 per cent.

The majority of the cases, namely 73, are in Group I. In 47 of these cases a history either of syphilitic infection was obtained or clinical manifestations thereof were found. Nine of the 73 women did not return to the clinic after their first visit and were not confined in hospital, so there are insufficient details from which to draw any conclusion. In the 17 women in whom no history of infection was obtained, nor manifestation of syphilis found, there was a repeated positive Wassermann reaction; in addition, in some women there was a suggestive obstetric history. The babies of four of these 17 women showed syphilitic manifestations; one had snuffles and three had syphilitic pemphigus. The ages of these four mothers respectively were 36, 22, 43, and 25 years; the first two were primigravidæ and the third was a 5-para—all her previous children were either still-born or died within seven days of birth; the fourth case was a 3-para, her first child was still-born, her second child was born at full time and was apparently healthy, but a Wassermann test was done and found triple positive; the third pregnancy terminated in a miscarriage at the fourth week. The Wassermann reaction was triple positive on three occasions in each of the primigravidæ during the antenatal period, and again in the blood of the umbilical cord and in the puerperal blood. Two other women of the 17 had repeated strong Wassermann reactions and a suggestive obstetrical history.

Case 2767 : age 31 years, para 4 : Wassermann reaction triple positive on 22nd June 1926; 9th September 1926, and again on 23rd September 1926 after a six months miscarriage. Past obstetrical history : C<sub>1</sub> full time (illegitimate, further history of

this child not known); C<sub>2</sub> premature (7 months) alive and well; C<sub>3</sub> premature (8 months) died aged 4/12 years; C<sub>4</sub> abortion at second month.

Case 1285. Age 30 years, para 7. Wassermann reaction triple positive on 22nd October 1925 and 16th September 1925 and negative (under treatment) on 16th October 1925 and 12th December 1925. Delivered on 10th September 1925 of a full time living child. Past history: C<sub>1</sub>, C<sub>2</sub>, and C<sub>4</sub> full time, alive and well; C<sub>3</sub> died aged 4/12 years. C<sub>5</sub>, C<sub>6</sub>, and C<sub>7</sub> full time stillborn.

Nine of the 17 cases had repeated positive Wassermann reactions as the only sign of syphilis. Three of the women were primigravidæ, two of the three were single girls aged 23 and 22 years respectively. The remaining women were all over 25 years of age. Four of these patients had had one previous pregnancy, two had had two previous pregnancies and one had had three previous pregnancies. Their obstetrical histories were good and did not suggest syphilis. In the interim report of the sub-committee of the Medical Research Council<sup>7</sup> examining the question of the value of the positive Wassermann reaction, it is suggested that when a positive Wassermann reaction is the sole evidence of syphilis, detected by a particular observer who makes the clinical examination, it should be repeated, and if still positive it may then be accepted as proof of syphilis. This suggestion, along with the findings of Boas, Gammeltoft and Siecke and the suggestion of F. J. Browne regarding the value of the Wassermann reaction in pregnancy, seems to justify the diagnosis of syphilis in nine cases with repeated positive Wassermann reaction.

The remaining two women of this group had a positive Wassermann reaction on one occasion only; they both came under observation in the last month of pregnancy, and after confinement were transferred to another centre for further observation. One of these patients was a multipara, 42 years of age, with a bad obstetric history—her first three pregnancies had ended in miscarriages at the third month, the fourth pregnancy went to full time but the child only lived ten minutes. The other patient was a primigravida aged 22 years. Her Wassermann reaction was doubtful positive on 19th April 1926. She was given a provocative dose of one of the arsenical compounds but did not return to the clinic until she was in labour. The blood of the umbilical cord and also the patient's blood on the third day in the puerperium were reported as triple positive. Both these patients were subjected to a thorough examination during the three months following their transfer from the Maternity Hospital and were found to be negative. The second case is interesting as there are two triple positive results. On looking up the particulars of this case one

found that the delivery was an instrumental one and that chloroform and ether anæsthesia was used. Chloroform is one of the drugs which exerts an influence on the Wassermann reaction; whether it had anything to do with the reaction in this case must remain a speculation. These two cases serve to remind one that the Wassermann reaction is not infallible and that even in the best laboratories mistakes may occur in the reading of individual specimens.

Twenty-six women in this group were traced to other venereal diseases treatment centres, all had been under observation there for not less than three months. In twenty-four cases the diagnosis of syphilis was upheld, the remaining two cases were negative as already reported. Six of the twenty-six cases had positive Wassermann reaction as the only sign.

Group II. There are six women in this group; two of these were in the early secondary stage when they came under observation—they each had a primary sore on the labium, inguinal adenitis and coppery polymorphous rash. A third woman was a known syphilitic, who had been under regular treatment for about 18 months before she became pregnant. Her Wassermann reaction was weak positive for one year before she became pregnant and during the first two months of her pregnancy, at the fifth month her Wassermann reaction was moderately strong positive and it remained so in spite of treatment during the remainder of her pregnancy. The fourth case in this group illustrates clearly the value of the routine use of the Wassermann reaction.

Case 2673. Age 23 years. Two previous pregnancies ended at full time, both children alive and well. Her Wassermann reaction was weak positive on 20th August 1926, and again on 28th August 1926 when a provocative dose of one of the arsenical compounds was given; delivered spontaneously of a full time child on 10th September 1926. Puerperal Wassermann reaction moderately strong positive. On examination on 28th August 1926 a healed scar was noted on left labium and the woman admitted having had a sore followed by a generalized rash and sore throat during her first pregnancy. The diagnosis of syphilis was confirmed after a thorough examination at the second treatment centre. The remaining two cases gave no history of infection and showed no specific manifestations.

Case 926. Age 26 years, para 2. Wassermann reaction moderately strong positive on 2nd October 1924 and 12th October 1924. Given treatment during the remainder of her pregnancy and delivered of a full time child. Past obstetrical history: C<sub>1</sub> stillborn; C<sub>2</sub> full time, alive and well. The remaining case was a primigravida aged 23 years. Her Wassermann reaction was

moderately strong positive on 15th July 1926 and 30th July 1926. Treatment was then given and Wassermann reaction was negative on 4th September 1926—four days after delivery.

Definite evidence of syphilis has been found in four of the six women. The number of cases in this group is too small for any general conclusion to be drawn, but from experience one would consider it advisable to repeat the Wassermann test and if it were still positive, then from the point of view of treatment one would look on the case as syphilitic.

Group III. This is perhaps the most interesting group, since most clinicians are reluctant to attach any importance to a reaction unless it is strongly positive; they fear a wrong diagnosis and, naturally, do not wish to attach the label "syphilis" to their patients, yet, when some clinical manifestations can be found in six out of 19 cases there seems to be justification for a more careful consideration of these cases. Further, it is well known that the type of syphilis met with in the pregnant woman is in a large number of cases latent; the degree of complement fixation in the Wassermann test appears to be dependent on the activity of the syphilitic lesion, but, until one knows what the modification is, which fixes the complement in the syphilitic serum, little can be said in explanation of the degree of fixation. From clinical experience one knows that in pregnancy in the majority of cases the more recent the date of infection the more likely it is for a miscarriage or premature birth to occur and the more distant the date of infection the more likelihood there is of a full time child being born.

This group contains 28 cases; in nine of these there are insufficient details owing to these patients not returning to the clinic. The remaining 19 cases were examined carefully and six considered to be negative cases, four were definitely congenital syphilitics, two were cases of latent syphilis; four were doubtful but their obstetrical histories were suggestive of syphilis and three cases, with negative obstetric history, were doubtful.

The two latent cases were elderly multiparæ—aged 36 and 32 years. The one showed signs of early tabes dorsalis and her three living children had each triple positive Wassermann reactions. The other woman had had three premature stillborn babies, followed by a full time child, which was apparently healthy. The ratio between fœtus and placenta was noted to exceed four. F. J. Browne<sup>8</sup> says a weight ratio of more than four in a full time child, in the absence of placental infarction or hæmorrhage, is suggestive of syphilis. This patient came under observation 18 months later when she was delivered of a macerated syphilitic fœtus and

her Wassermann reaction taken on the fourth day of the puerperium was triple positive.

In the four doubtful cases with suggestive obstetrical history the women were, with one exception, 32 years of age. They all had had stillborn children, and either miscarriages or premature children, who died within a few days of birth. These women would require to be kept under observation for some time before a definite diagnosis of syphilis could be made.

The three doubtful cases were aged 20 years, 25 years, and 33 years; the first was that of a primigravida, the other two were multiparæ, para 2 and para 1. The primigravida was a sister of the last case mentioned in Group II. Their family history was gone into but nothing suggestive of congenital syphilis was elicited.

The Wassermann reaction in all these cases was taken on more than one occasion. It is unfortunate that only two cases were traced in this group as one feels that a diagnosis had not been arrived at.

J. S. Lawrence<sup>9</sup> investigated the clinical significance of the incomplete Wassermann reaction in 839 cases. In a group of 251 cases with a weak positive reaction he obtained clinical symptoms in 70 cases and a suggestion in another 22 cases.

Summarizing the cases with weak positive Wassermann reaction; there were actually 30 cases in which this result was reported at the first examination. In one case the Wassermann reaction became triple positive after a provocative dose of one of the arsenical compounds. This woman has since been under observation at a treatment centre for three months and is considered to be syphilitic. This case is included in Group I. A second case with a weak positive reaction followed by a moderately strong positive is fully reported in Group II. Six cases had a negative Wassermann reaction on the second occasion when it was tested and again after a provocative dose. In ten cases the Wassermann reaction was weak positive on more than one occasion; in four of these after a provocative dose. In one case the reaction became doubtfully positive after a provocative. Nine cases were insufficiently investigated. These findings, together with those of J. S. Lawrence, justify us in regarding the weak positive reaction with suspicion of syphilis.

Group IV. In 17 cases the Wassermann reaction was reported to be doubtful positive. Twelve of these had the test repeated—four after a provocative dose of the arsenical compounds—with a negative result. Five of these were not investigated as they did not return to the clinic. No history of infection and no clinical manifestation of syphilis were found in any of the cases investi-

gated. From these findings one did not regard the doubtful positive reactions as of any significance. Another case which had a doubtful reaction at the first examination is fully reported in Group I.

Group V. Six cases were reported to have anticomplementary sera. Some observers say that this type is more frequently met with in pregnancy than at other times. It had no significance clinically as far as was observed from these cases.

Group VI. There were 15 cases with a negative Wassermann reaction but with clinical evidence of syphilis. Three women had primary sores on admission; four women were congenital syphilitics, all of whom had had some, but irregular, treatment; three women had been under treatment when they become pregnant and were transferred to the Maternity Hospital; one woman had numerous gummata over the right thigh, on both labia and around the anus; these cleared up rapidly under antisyphilitic treatment; two women showed no signs of syphilis but their children were attending for anti-syphilitic treatment, although the mothers refused treatment for themselves; the remaining two women were delivered of macerated foetuses, who showed secondary evidence of syphilis.

#### CONCLUSION.

Attention has been drawn again to the frequent absence of history or clinical manifestations of syphilis in the pregnant woman; to the high percentage of stillbirths and deaths under one year of age from syphilis, and to the preventable character of this cause. It has been shown in the present series that the first evidence of syphilis, and in some cases the only evidence, was a positive Wassermann reaction. There is little doubt but that several of these cases would have been missed if the Wassermann test had not been applied as a routine procedure. The urine of the pregnant woman is examined for albumin as a routine and silver nitrate is instilled into the eyes of the newborn babe as a routine and many tragedies are thereby averted; many more can be averted by the routine examination of the blood, with the additional aid of a provocative dose of one of the arsenical compounds, if necessary.

The need of a fuller investigation and "following-up" of cases with incomplete Wassermann reaction is shown.

In conclusion, it is a pleasure to acknowledge my indebtedness to the Physicians of the Royal Maternity Hospital, Edinburgh, for access to the case records in the Hospital and to Professor F. J. Browne, for access to ante-natal records.



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