THE MANAGEMENT OF THE SYPHILITIC MOTHER IN PREGNANCY

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THE diagnosis of syphilis is never more important than in pregnancy. Prompt and adequate treatment is not only therapeutic, but prophylactic also, whereas neglect or delay condemns both mother and child to the ultimate effects of the disease. However, it is common experience that pregnant syphilitic women are most reluctant to attend for treatment, and it is thought that this is because they have to go to the ordinary veneral disease clinics to be treated. For this reason the treatment of syphilis during pregnancy should, as far as possible, be carried out in the antenatal clinic or maternity hospital and should be regarded as an integral part of maternity and child welfare. It is much easier to induce the pregnant woman to come to the ordinary antenatal clinic where no difference is made between herself and the other patients, and where she receives the treatment unobtrusively.

The Diagnosis of Syphilis in Pregnancy.

At the first antenatal examination a careful enquiry and clinical examination followed by the Wassermann reaction and Kahn test will detect any evidence of syphilis. A patient with clinical findings suggestive of the disease, and with a positive Wassermann reaction and Kahn test, needs no further investigation; treatment should be started immediately. The problem arises when the clinical signs and the serological tests fail to support one another. As the value of a routine Wassermann reaction and Kahn test is now recognized widely in antenatal work, a knowledge of the factors which may produce misleading results is essential for the interpretation of findings and for the evaluation of each case.

The value of any serological test in the diagnosis of syphilis depends on its sensitivity and specifity and, while the modern Wassermann reaction has reached a remarkable degree of accuracy, neither sensitivity nor specifity is absolute. A clear-cut positive reaction is not obtained at every stage and in every case of syphilis, while non-specific or false positive reactions may be found in non-syphilitic patients. A negative Wassermann reaction may occur up to 8 weeks after infection, but in secondary syphilis the Wassermann reaction is almost invariably positive. In late untreated cases and in congenital syphilis negative serological findings occur in a small percentage of cases; in syphilis under treatment the Wassermann reaction becomes negative long before the disease has been cured.

The ingestion of alcohol, or chloroform anaesthesia, may temporarily convert a true positive Wassermann reaction to negative, but this change does not persist for more than three days.

While a true positive serological test is obtained almost exclusively from cases of syphilis, a false positive reaction may occasionally be found in certain well-defined groups of conditions. These are

usually caused by organisms which possess antigenic properties very similar to those of *T. pallidum*, and include rat-bite fever, Weil's disease, typhus, vaccination, cerebro-spinal fever, typhoid, leprosy, tuberculosis, malaria.

There are a number of intercurrent conditions which may also give a non-specific positive reaction, such as beri-beri, pellagra, cancer, diabetes mellitus and pregnancy.

False Positive Serological Reaction in Pregnancy.

Frequency. In a summary of numerous investigations Kolmer and Tuft (1941) state that false positive serological findings during pregnancy vary from 0 to 1.9 per cent. Stokes (1934) gives his figures as varying between 0.5 and 3.8 per cent.

Penttinen (1946) reported the Wassermann and Kahn reaction in 20,145 women. He concluded that pregnancy in itself does not interfere with the reliability of these tests. False positive results appear in pregnant as well as in non-pregnant women. Although the incidence of false positive results in a large series of unselected cases was small, the percentage of the positive cases which were falsely positive due to pregnancy was relevantly high; 21.5 per cent of all the positive reactions were misleading, and so were at least 28 per cent of the tests of the cord blood, so that the importance of the false positive reaction should not be underestimated.

Poeck (1927) reports that during the first 4 months of pregnancy there was not a single non-specific positive reaction, but in the 5th month 3 per cent, in the 6th month 3.4 per cent, in the 7th month 3.8 per cent, in the 8th month 6 per cent, in the 9th month 4.7 per cent, and in the 10th month 6.2 per cent of cases gave false positive results.

Causes. Attempts have been made to explain the occurrence of false positive serological findings in pregnancy by reference to various technical details, and to certain biochemical and physico-chemical changes which are found in the blood.

(*a*) *Technical.* In the literature there are a number of accounts of technical details which produce false positive results when Wassermann and Kahn tests are performed on blood samples collected during pregnancy.

Finkener and Neugarten (1924) emphasize that prolonged conservation of serum increases the number of false positive results, especially when retro-placental blood is used.

(*b*) *Physiological.* Besides such technical factors as are mentioned in the literature there have been numerous attempts to explain false positive results during pregnancy (Haim, 1927). The explanations are usually based on the fact that the Wassermann test cannot be considered as a true specific serological reaction, and it has been suggested that many variations in the composition of the blood might have an influence on the results.

Georgi and Handorn (1923) speak of increased lability of the plasma during pregnancy, when technical factors can produce a false positive reaction more easily than usual. Czyzewicz (1929) uses the expression "quick decomposition in changed metabolism" in explanation of false positive results observed by him. Laubenheimer (1930) considers the increase in the lability of serum globulins which takes place during pregnancy to be the cause of false positive results, especially during the later months of pregnancy.

Forssman (1932) mentions pregnancy as one of the conditions in which the increased quantity of globulin in the serum can give rise to a positive Wassermann reaction.

Esch (1922) and de Candia (1928) are of the opinion that the numerous false positive reactions observed by them can be explained in the first place as a manifestation of disturbed lipoid metabolism, since it is known that the level of blood cholesterol during pregnancy is higher than normal. Belding (1925) and Schäfer (1935) both consider it proved that the serum of pregnant women contains 8 times more anti-complement non-syphilitic substances than that of non-pregnant women.

Sabatelli (1942) has examined the matter experimentally and, by absorbing the non-specific positive serum of a pregnant woman by extracts from ovaries, placenta, and hypophysis, has arrived at the result that non-specific positive reactions are produced by antibodies reacting with lipoids from these organs.

Negative Serological Findings in Pregnant Syphilitics.

It is also maintained, on the other hand, that pregnancy causes the reversing of true positive serological reactions for syphilis into negative ones. Laffont and Melé (1928) have reported that in general about 66 per cent of non-pregnant syphilitics give a positive Wassermann, while during pregnancy the percentage is only 32 to 38.5. During re-examination of those mothers after delivery, they obtained more serum-positive cases than at the time of pregnancy.

Czyzewicz (1929) is of the same opinion, and bases it on the circumstance that only 84 of the mothers of 166 syphilitic children had a positive Wassermann at the time of pregnancy. Vignes (1928) states that the evaluation of serological tests for syphilis during pregnancy is more difficult than usual because the true sero-positivity becomes reversed and the non-specific sero-positivity appears.

Finally Nevinny (1933) considers that the problem during pregnancy is not the obtaining of false positive results, but is that in spite of serological investigation so many cases of syphilis remain undetected during pregnancy.

The Treatment of Syphilis in Pregnancy.

There is seldom such a unanimity in the literature as is found in regard to the importance of antisyphilitic treatment of the pregnant mother for the prevention of syphilis in the child.

Soloway (1945) states that treatment of syphilis in the mother is the most effective prophylactic method of medical science. The following findings have been established with full certainty on the basis of numerous investigations (Baos, 1927; Gammeltoft, 1928; Klaften, 1929; Daily, 1944).

1. The treatment of the syphilitic mother is always indicated, no matter how far the pregnancy is advanced.

2. Women treated both before and during pregnancy yield fewer syphilitic children than either of the groups separately.

3. The best results of treatment during pregnancy are obtained when started before the 24th week.

4. Bismuth and the organic arsenical compounds must be used; the use of the latter is especially important during the later weeks of pregnancy.

Organization of Treatment.

All antenatal patients have a routine serological test carried out on first examination. If a positive result is reported the patient is interviewed and questioned about any history of the disease or previous treatment, and the serological test is then repeated.

Once the diagnosis of syphilis is made the patient is admitted to hospital, and is given 5 mega units of penicillin over a period of 5 days, 5,000,000 units night and morning.

On completion of the penicillin course, weekly injections of arsenic and bismuth are given, in the first week 0.3 g. Neoarsphenamine intravenously and 0.2 g. bismuth intramuscularly, and the second to tenth week inclusive 0.45 g. Neoarsphenamine and 0.2 g. of bismuth. The Wassermann reaction is done after one month's rest, and the course of arsenic and bismuth is resumed. The cycle is repeated until 14 days from term, but if there is any idiosyncrasy to arsenic only bismuth 0.2 g. weekly is given.

It should be stressed that a positive Wassermann and Kahn test does not mean that the patient is infective. She is infective only if she has early lesions—a primary sore or secondary signs. Both medical staff and nurses are far too prone to regard a patient with a positive Wassermann as one who may infect them, and they demand her admission to a V.D. Department. We are of the opinion that all mothers with a history of treated syphilis, whether they have a negative or positive serological test, should be treated throughout pregnancy.

With mothers treated after the 4th month to term, the babies have treatment and observation from birth for 2 years, regardless of whether the Wassermann reaction of the cord blood was negative or positive, as the testing of the cord blood at birth to diagnose infection of the child is not reliable. A positive result does not necessarily mean infection, since it may occur from a carry over into the placental circulation of the mother's positive reaction. On the other hand, a negative result cannot be taken as meaning that the child has escaped infection, as a positive reaction may appear any time up to 6 months after birth, and in fact the diagnosis of congenital syphilis in the child is not always easy because of this. Where physical signs are present the diagnosis is not difficult; it is the children of mothers who have started treatment later than the 4th month of pregnancy that may not present physical signs of the disease, and these infants should be treated soon after birth.

Experience has shown that where the mother has started treatment before the 4th month and has continued throughout the pregnancy, the baby is almost invariably free from syphilis.

The penicillin dosage for babies is based on a formula age/age + 12. This is followed immediately by weekly injections of sulpharsenol in aqueous solution mixed with bismuth-oxychloride. The sulpharsenol dosage is 10 mg. per 2 pounds body weight; and the bismuth solution would be estimated on the same formula—1/1 + 12. After a ten-weeks course of sulpharsenol and bismuth oxychloride there is a rest of one month, and during this time a tonic, syrup ferri iodide, is given.

After a month's rest, another serological test is done and the course of sulpharsenol and bismuth is repeated.

Case Report

During 2 years we have treated and delivered 30 pregnant syphilitic women. There were 29 live births and 1 stillbirth. There were no abortions and no neonatal deaths.

That the stillbirth was not due to syphilis was confirmed by postmortem examination, and there was no pathological evidence of the disease in the infant.

In the 29 live births there were no prematurely born infants. For the most part, the mothers were young primigravidae with a recently acquired infection. The oldest pregnant woman we have treated was 41 and the youngest 18.

Twelve of the 30 patients had received no previous treatment for syphilis and 18 had received some treatment prior to pregnancy. All the 30 patients had 5 million

Oxford units of sodium penicillin; 14 received more than 10 injections of arsenic and bismuth and 16 patients less than 10 injections during pregnancy.

Initial treatment was given in various stages of the pregnancy. Prior to the 24th week—13 cases; between the 24th and 32nd week—12 cases; after the 32nd week—5 cases.

Since foetal infection is considered to occur any time after the 24th week, and to become increasingly more probable as term approaches, the distribution of cases throughout the pregnancy as indicated should give a fair indication of the value of treatment in any stage.

The only reaction of note encountered was, in one case, lower abdominal pain and slight vaginal bleeding at 36th week of gestation, but the patient subsequently had a full-time normal delivery.

The postnatal medical follow-up has consisted of a cord Wassermann and Kahn test and a roentgenogram of the long bones. A complete physical examination is also performed. Three of the 29 infants born alive and physically normal had a positive blood serological test at birth, and in every instance the mother was also seropositive at the time of delivery.

All roentgenograms of the long bones performed in the nursery have been normal. Physical examinations have shown no evidence of syphilis.

What should be the ideal follow-up of the Infant?

(1) The infant should have a complete examination, including a Wassermann reaction and an X-ray of the long bones, in the neonatal period.

(2) If clinical signs of syphilis are found, or if a positive Wassermann reaction is present, treatment should be started, and a quantitative test repeated monthly to determine the trend of the disease. Treatment should be continued until one course has been given, and, if there are no clinical signs and a negative Wassermann reaction, it should be stopped and the child followed up at 6-monthly intervals up to 2 years.

(3) Infants with a negative Wassermann reaction should have blood tests monthly for the first 3 months, and then 6-monthly until 2 years of age. No infant born of a syphilitic mother should be considered free of syphilis until clinical examination and serological test and radiological findings have been consistently negative for 2 years.

Treatment of the Mother in Later Pregnancies.

The literature in this country and abroad contains repeated recommendations that the syphilitic mother should be given adequate treatment in every pregnancy and, fundamentally, the decision depends upon the ability of penicillin, arsenic and bismuth to cure syphilis. Obviously if the expectant mother has not been cured of her syphilis by the previous treatment, there is no question that re-treatment during each pregnancy is essential.

Cole and his co-authors (1934) reported that in a group of 50 syphilitic women considered cured, no syphilitic child resulted from subsequent pregnancies during which no treatment was given. Stokes (1934) advocates the treatment of the syphilitic woman through every pregnancy regardless of the duration of her infection, her serological status or the amount and type of therapy; but adds the comment that some modification of this position may be possible when reports are available of an extensive series of mothers clinically cured of the disease who have gone through subsequent pregnancies untreated. Moore (1941) states that re-treatment of a previously treated mother may be safely omitted if the mother's infection is of more than 10 years' duration; if previous treatment has been adequate and, especially, if

several uneventful and sero-negative years have passed by since the termination of treatment or if one or more preceding pregnancies, during which the mother has been allowed to go untreated, have resulted in living children known to be non-syphilitic. He feels that, if at least 2 of these 4 criteria cannot be satisfied, it is safer to treat the mother during the pregnancy in question, in spite of the fact that her own blood tests may be repeatedly negative. McKelvey and Turner (1934) agree that thorough treatment of the maternal syphilis prior to pregnancy probably affords adequate protection of the offspring in subsequent pregnancies even though treatment during pregnancy is omitted; but advise that, if the maternal serological test remains positive, or if there is clinical evidence of persistent infection, the mother should be treated during every pregnancy regardless of the amount of previous treatment.

To sum up, in the days before penicillin, women considered as cured of syphilis by arsenic and bismuth often gave birth to normal infants without treatment during their pregnancy. But, as a general rule, re-treatment in each pregnancy was considered necessary to ensure a healthy child. As it is still doubtful whether even the present methods of treatment are the complete answer to syphilitic infection, and with so much at stake for the child, one hesitates to go against the firmly established principle of treating the mother during each and every pregnancy.

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