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SYPHILIS AND PREGNANCY

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Syphilis was recognized centuries ago among those skilled in the Medical Art of their time. Buret claims it was known to the Chinese and it seems evident that it was also known to the Japanese, Jews, Assyrians, Egyptians and Babylonians. Many historians believe that the disease was indigenous in South America and that its introduction into Europe was brought about through the sailors first accompanying Columbus to the new world. In any event the appearance or recognition of the disease in Europe dates from 1494.

In 1502 Almenar thought the disease was incurable and inevitably transmitted to the offspring. Forella early in that same century observed that infants were often infected at the breast. Paracelsus, in 1529, stated that syphilis could be transmitted from the father to the infant.

Pare, in 1533, wrote the first clear conception of congenital syphilis, when he wrote that "infants oft times conceive the seeds of this disease in the wombs of their mothers and are born infected, wherewithal pustules presently arising over all their bodies." Fallopius, in 1555, added to this by saying, "you will see small children, born of infected women, who suffer from the sins of their parents, and who are born in a semicooked condition."

In the latter part of the 16th century, Colles compounded his law which has come down through the centuries. He stated that "a healthy, nonsyphilitic mother can give birth to a syphilitic child." Profeta also came forth with his statement that "apparently healthy children of syphilitic mothers do not develop clinical syphilis through contact with such mothers, even though suckled by them."

The first appearance of syphilis to the North American Colonies was in Boston in 1646. John Winthrop recorded, "A certain sailor infected his wife and neighbors resorted to her; some of them drew her breasts and others let her children suck them and sixteen persons were thus infected." It was further observed that none took of the disease except by copulation or suckling.

In 1738, Astruc stated that, "There are some, however, whom I forebear now to spend time in imputing, who think the Venereal Poison is nothing else but a numerous school of little nimble brisk invisible living things, of a very prolific nature, which when once admitted, increase and multiply in abundance, which lead frequent colonies to different parts of the body, and inflame, and exulcerate the parts they fix on.....in short which without any regards to any particular quality of any humour, occasion all the symptoms that occur in the Venereal disease." Thus he gave a clear description of congenital syphilis, but missed the true significance of his observation.

In the nineteenth century John Hunter inoculated himself with the pus from a patient with gonorrhea and acquired both diseases. This caused a great deal of confusion regarding the specificity of the disease. Even though Hunter gave the classical description of the primary lesion, he inhibited the progress of discovering the actual causative agent, by his experiment. In 1828, Hutchinson gave us the classical descriptions of congenital syphilis.

Not until 1905 did we know the true cause of the disease, and it remained for Schaudinn to discover and describe the causative organism.

Hoffman confirmed the results and Metchinkoff was the first to produce the disease in a laboratory animal, when he inoculated a chimpanzee with the disease.

The next real step and the one which revolutionized the therapy of syphilis came after the long diligent work of Ehrlich and his discovery of "606". Probably no other one discovery has so effected the progress of mankind, for it opened to the world a method of cure for syphilis but also opened the wide field of chemotherapy.

INCIDENCE OF SYPHILIS IN PREGNANT WOMEN

Syphilis as a disease is by far less common in occurrence in the United States than it is in most of the European countries, and to us in the Midwestern States it is less common than in the Southern and Eastern States, where the negro population is greater.

The figures and percentages of occurrence as a disease complicating pregnancy also vary widely. Williams, in Baltimore, reported in 1920 that the incidence averaged 2.5 per cent for the whites and 16.3 per cent for the colored race. Moseley at Duke reported in 1940 their figures which were 0.8 per cent for the white race and 7.6 per cent for the colored race, although the percentages ran higher when comparing the general incidence at the Duke Hospital. These figures were 3.2 per cent for the whites and 32 per cent for the negroes. Holloran of Los Angeles recently reported the occurrence of syphilis in pregnancy in their hospital was 2.04 per cent, from records of better than 35,000 pregnancies. Jeans and Cooke in St. Louis found the distribution of syphilis among the

pregnant women of the poorer class about 5.7 per cent, as compared with about 1.0 per cent in the higher classes. From the records of the Wisconsin State Board of Health for the year 1941, it is found that the percentage of syphilitic pregnant women was only 0.1 per cent, regardless of color or class distinction. This represents the percentage of positive blood Wassermanns found in the 26,967 pregnant women who were tested for syphilis and this total number of women tested represents 48.2 per cent of the pregnant women in the State for that year.

SEXUAL DIFFERENCES IN THE DISEASE

It has long been recognized that syphilis in the female differs from the same infection in the male.

The occurrence of the disease is nearly the same regardless of the sex, but because of the anatomical structure of the female the primary lesion is often missed by the women when it lies within the vaginal canal, on the cervix or within the uterus. Furthermore, the primary lesion tends to be smaller and of a milder nature in the female.

The secondary lesions are usually of a much milder nature in the female and they are often so slight as to be missed or they may not appear at all. However, associated with this the women tend more often to show constitutional symptoms and exhibit a low grade toxemia, general malaise, nervousness, poorly defined gastric symptoms, menstrual disturbances, a well marked secondary anemia and a slight relative and absolute lymphocytosis.

As the syphilitic infection progresses beyond the secondary stage

it tends to become latent in women, especially in those in the child bearing age. In the latent stage the women are symptom free and in general good health. The occurrence of cardio-vascular involvement is rare in women, but more frequent in men. The lesions of the liver in the form of gumma are rare in occurrence, but seem to appear more often in women than in men. The spleen, likewise rare in involvement, is more frequently involved in women. Syphilis of the stomach is not infrequently involved in males, but rarely so in females. The involvement of the ovaries has been seen by so few that for all practical purposes it may be said that it never occurs. Occasionally the pancreas or adrenals may be the seat of a lesion in females, as may a gumma of the rectum. The involvement of the central nervous system is four times more common in males than it is in females.

INFLUENCE OF PREGNANCY ON THE DISEASE

As early as 1810 Bertin noted that syphilis is apt to run a rather benign clinical course in women and in part attributed it to parturition when he remarked, "The pregnant state modifies them and causes them to disappear spontaneously."

It has come to be generally recognized that pregnancy causes a marked effect upon the disease. Ingraham says, "The diagnosis offers under the most favorable circumstances a problem fraught with difficulties, becomes manifoldly harder when we are dealing with the disease in pregnant women, for here we have to do in the vast majority of cases with the almost symptomless and none too well understood period of latency."

It has been observed by many that if infection occurs about the same time as impregnation, the primary and secondary lesions are often completely suppressed, or if present are milder in degree than in the nonpregnant woman or in men.

This beneficial effect of pregnancy upon the syphilitic infection often extends throughout the life time and the woman rather continues to have a symptomless latent type of infection, and seldom progresses to the later or central nervous manifestations. Moore has gone so far as to say that a properly controlled pregnancy may be a valuable therapeutic measure in the treatment of syphilis in women, enhancing the probability of an ultimately favorable outcome.

EFFECT OF SYPHILIS ON PREGNANCY

The effects of syphilis on the pregnancy are very striking and the greater percentage of the pregnancies of syphilitic women end disastrously, unless treatment is instituted.

Williams stated that before modern therapy, syphilis was the most common cause of stillbirth and that it accounted for three-fourths of the macerated fetuses and even larger numbers of children with congenital syphilis. Moore said "34 per cent of all fetal deaths were due to syphilis before arsenical treatment came into light". He further adds that in the untreated women with latent syphilis, only 16.9 per cent give birth to living nonsyphilitic infants, whereas 11.1 per cent were living but had congenital syphilis, 18.4 per cent died in infancy, 48.9 per cent resulted in miscarriages or stillbirths, and 4.5 per cent in abortions.

Mc Cord says an untreated syphilitic pregnant woman has only a 35 per cent chance of having a living nonsyphilitic child. Holloran, in Los Angeles, reports in untreated women 68.75 per cent have living syphilitic children, 12.5 per cent end disastrously and only 18.75 per cent have living nonsyphilitic children. Mc Kelvey and Turner report a series of 286 untreated syphilitic pregnant women who delivered only 54.1 per cent living infants, while 45.9 per cent were stillborn. Of the living infants 64.5 per cent were shown to have congenital syphilis. Jeans presented the figures as 16.6 per cent living nonsyphilitic infants, 30 per cent miscarriages or stillbirths, 30 per cent died in infancy, and 24 per cent were living but had congenital syphilis. From Johns Hopkins Hospital report of 1,000 consecutive fetal deaths in the past ten years it was found that ten per cent are still due to syphilis.

It is generally accepted that the chances of syphilis being passed on to the child are greatest if the disease is acquired shortly before, at the time of or soon after conception. If the infection occurs after the sixth month, the child will presumably be normal. It was found that thirty-one per cent of the women with early syphilis who had a positive blood Wassermann bore syphilitic infants and as the duration of the infection increased and the disease became latent before conception, the transmission of syphilis to the child decreased to 18.8 per cent. Thus it may be said that the probability of transmission in utero diminishes as the number of years between the infection and the pregnancy increases. These statements do not mean that under the conditions stated, treatment may be omitted with complete safety to the child.

PATHOGENESIS OF SYPHILIS IN THE PREGNANT WOMEN

Much has been written on the pathogenesis of syphilis in the pregnant woman. As early as 1529, Paracelsus stated that syphilis could be transmitted from the father to the fetus. This same opinion became the basis for Colles' Law. However, in order to believe in this law, one must except the fact that the spirochete is carried to the fetus by the spermatazoa and does not invade the maternal system. Knowing the relative size of a spermatazoa and a spirochete we must assume, as is so aptly put by J. W. Harris that the little sperm shoulders the mighty spirochete and carries it through the cervical and uterine canal to the ovum. We must consider the possibility of this route of infection if we believe that there is a spore or microgranular form of the spirochete.

There are some workers who believe that the spirochete in infected semen may pass into the uterine cavity after intercourse, and traverse the decidua capsularis to directly infect the fetus. This mode of infection has never been demonstrated.

The most common and the only method of infection that, for all practical purposes, needs be considered assumes the original infection in the mother, with a subsequent spirochetemia sometime during her nine months of pregnancy. In this manner the organisms are carried by the blood stream to the placenta where they lodge, and may form a thrombus which results in an infarct and through this weakened area pass on over to the fetal portion of the placenta and to the fetus itself. It has been shown by some that the organisms may penetrate a normal vessel wall and pass into the fetus without the infarct stage.

Through the long continued study of the mode of infection of the fetus, it has been shown that the organisms are never present in the fetus before the fourth month and in most cases the appearance is delayed until the sixth, seventh or eighth month. The reason that the spirochetal invasion of the fetus does not take place early can best be explained by the fact that the protective Langhans cell layer is present during the early months of pregnancy and does not begin to atrophy before the fourth month, and it is not until the sixth month that it disappears. This layer of cells combined with the very effective placental membrane seems to prevent the passage of the organisms into the fetus. After the sixth month when the Langhans layer disappears the most effective protective mechanism is removed and the spirochetes invade the fetal portion of the placenta.

It must be fully realized that the placental membrane itself offers a great deal of protection to the fetus, when we recognize the fact that one-fifth to one-sixth of the children born of syphilitic mothers will be normal in spite of prolonged exposure to the disease.

It has been shown by Mc Cord that when fetal death occurs, it is the result of inadequate blood supply to the placenta due to blockage of the placental vessels.

DIAGNOSIS OF THE DISEASE IN PREGNANT WOMEN

The diagnosis of syphilis in the pregnant woman is not without its difficulties, for the disease is usually symptomless. Ingraham states that from seventy-five to eighty per cent of these women will present no

symptoms even to careful and complete examination, from which a diagnosis could be made or the disease even suspected, and many in whom syphilis was discovered will profess total ignorance, not only of the source of the infection or the time of its inoculation, but even of any abnormality in themselves that they might attribute to the disease. Halloran, in Los Angeles, in a report on 969 syphilitic pregnant women, says that only 52.73 per cent gave even a suspicious history of the disease and only 4.4 per cent presented any clinical evidence to careful examination.

In spite of the low percentage of cases that can be suspected by a careful history and physical, this means should not be slighted. Of particular interest is the obstetrical history of the women. A history of stillbirths, premature births, births to children who died shortly after birth, and even of repeated abortions, is of great importance.

The blood Wassermann has come into the foreground as a diagnostic measure, as eighty to ninety per cent of syphilitic pregnant women will have a positive blood serologic test. This simple test should be done routinely on every pregnant woman who presents herself for prenatal care. Idem, in Boston, showed in his series of five thousand maternity patients who were examined routinely that only 2.2 per cent ever showed suspicious signs of syphilis, while by routine blood Wassermann 9.2 per cent were shown to be syphilitic.

The validity of the blood Wassermann in pregnant women has been frequently challenged, but it is most generally agreed by such men as Mc Cord, Moore, Ingraham and Mc Kelvey that pregnancy does not cause false positive reactions. Occasionally pregnancy may cause a false negative

reaction and it is these cases where a careful history and physical and even examination of the other members of the family where the history is suspicious will prevent the physician from overlooking positive cases. In these cases the Wassermann should be repeated at frequent intervals to make sure of the reaction, in fact, any women with a negative Wassermann at her first prenatal visit should be checked at least once at the sixth to the eighth month.

Moore says that a strongly positive blood Wassermann in the pregnant women, verified on repetition, is diagnostic of syphilis regardless of the presence or absence of a history.

DIAGNOSIS OF SYPHILIS IN THE INFANT

A discussion of this subject is seemingly out of the realm of the general subject under consideration. However, if we stop to realize that basically whether or not a living, non-syphilitic child results from the pregnancy is the ultimate standard upon which we are able to judge the effectiveness of our treatment; then a discussion of this subject assumes a paramount place in this article.

The cord Wassermann has aroused considerable discussion and controversy. It may be generally said that even though the cord Wassermann is not absolutely reliable, it may be used to indicate the necessity for further follow up. It has been shown by Moore that a child with a negative cord Wassermann is five times as likely to be normal and only one-fifth as likely to develop other evidences of congenital syphilis, as is one whose cord Wassermann is positive.

The venous blood Wassermann taken shortly after birth likewise is not without its discrepancies, as it may also give false positives or false negatives. If the child of seropositive mother exhibits a positive blood Wassermann the chances are eighty per cent that he will be syphilitic and only twenty per cent that he will be normal. In other cases where the mother is seropositive but the child is seronegative, the child will actually be syphilitic in about thirty-six per cent of the cases. If the child who is free from the disease has a positive blood Wassermann at birth, this reaction will rapidly become reversed and even by three weeks fifty per cent will be negative. However, if a child who is infected with the disease presents a negative reaction at birth, the titre will gradually increase and become strongly positive by the sixth to eighth week, ninety per cent becoming positive by the third month. Therefore, if the blood Wassermann be followed for six months following delivery one is almost certain to pick up all cases of congenital syphilis.

The examination of the placenta has frequently been used as one means of discovering congenital syphilis. The gross examination of the placenta is at best a very poor method of recognizing anything but the far advanced cases of syphilis. The microscopic examination is of much greater value. Moore states that only twenty per cent of children with a normal placenta will ultimately develop syphilis, whereas eighty-eight per cent with evidence of a syphilitic placenta show other signs of syphilis ultimately and twelve per cent fail to develop any signs of congenital syphilis.

The Roentgenographic study of the long bones of the infant may also

be used to diagnose the disease. Here the presence of the osteochondritic process is characteristic and is usually evident within two to four weeks. This method of diagnosis is especially valuable when combined with the blood Wassermann reaction, where the seropositive infants are x-rayed the diagnosis may be definitely established within the first few weeks of life.

There have been numerous other procedures used to diagnose early congenital syphilis, which are not used very extensively. The dark-field examination of scrapings from the wall of the umbilical vein is not very extensively used. Although a negative result does not exclude the possibility of infection in the child, the finding of the micro-organisms from the scraping establishes the earliest and definite diagnosis of congenital syphilis.

The demonstrating of the organisms in the placenta is a very difficult procedure and the results obtained are not diagnostic unless the organisms can be demonstrated.

When all other methods of diagnosis of congenital syphilis lead to no definite conclusions, a clinical follow-up of the case remains as the best method. We must remember that the ideal time to recognize and treat congenital syphilis is immediately after birth and not at six months or a year. For this reason it is desirable to first use all the methods available for early diagnosis and if these fail to give the diagnosis, then a clinical follow-up remains as the only method.

THE TREATMENT OF SYPHILIS IN PREGNANCY

The treating of the syphilitic mother to preserve her child is reputed to have been first advised and carried out in France in about the middle of the seventeenth century. Garnier believed that treatment with mercury rubs even to the point of salivation far from harmed the gravid women and would cure them and the children. Mauriceau, using this method of therapy, reports the birth of healthy children. The prophylactic treatment of congenital syphilis first began to be used in this country in about 1870, as evidenced by a report of three cases where therapy with mercury proved effective.

The advent of the arsphenamines has increased the chances of a syphilitic mother having a living healthy baby from about thirty per cent to a figure in the neighborhood of eighty-five to ninety-five per cent.

The manner in which antisyphilitic therapy prevents the spread of the infection from the mother to the child still remains somewhat a matter for speculation. It has been shown by various investigators that the arsenicals and heavy metals do reach the fetus in at least minute quantities. If the work of Snyder and Speert in 1938 upon rabbits can be transfered over to the human then we may assume that the placental barrier and Langhans layer have much the same effect upon the passage of the molecules of the arsenicals and heavy metals through to the fetus, as they do upon the spirochetes themselves. These workers found that no arsenical could be found in the fetus until the period of viability was approached. Thus, we may say that the placental function, as measured by its capacity to transmit arsenic from the mother to the fetus, varies with the stage of pregnancy, the rate increasing as the pregnancy progresses. In trans-

lating these findings we realize that as the Langhans layer of cells disappear, arsenic will pass through the placenta to the fetus. It was further observed that the arsenicals were stored in the placenta and gradually liberated to the fetus, as indicated by the finding of greater amounts of arsenic in the fetus twenty-four hours after maternal injection than after one hour. And finally Snyder and Speert demonstrated that the concentration of arsenic in the fetus near term approached the level calculated to be present in maternal tissues when a definite antisyphilitic effect is exerted.

Thompson reported in 1941 that if pregnant women near term were given sobisminol orally the blood level reached a maximum in about two hours and then gradually tapered off to return to normal in eight hours. Likewise he found the fetal level reached a maximum in the same time and tapered similarly. The blood levels in the fetus were not as high as the maternal levels, but in some cases closely approximated them.

Eastman, at Johns Hopkins Hospital, showed that following antenatal arsenical therapy, arsenic is retained by the human placenta over periods as long as fifteen days after the last injection. The duration of this retention is conditioned in part by the number of weekly injections the patient has had, a definite cummulative retention of arsenic being manifest. He showed that the retention of arsenic by the placenta occurs chiefly in the fetal portion, three to four times the qusntity demonstrable in the maternal portion. This arsenic which is deposited in the placenta is not necessarily therapeutically active, but it remains certain that it exerts some therapeutic effects. In some later investigation

Eastman was unable to demonstrate any arsenic in the fetal blood following intravenous injection of arsenicals to the pregnant woman, although large quantities may be present in the maternal circulation. He found, however, that arsenic was constantly present in the meconium of newborns in those cases in which the mothers had had arsenical therapy during pregnancy. From these investigations he has concluded that the arsenic is stored in the placenta and gradually liberated to the fetus in small amounts.

Many investigators, as a result of the fact that arsenic is stored in the placenta, feel that the therapeutic action of the arsenicals results by preventing the spirochetemia in the mother and by destroying the organisms at the portal of entry: the placenta.

The ultimate aim in the treatment of syphilitic women during pregnancy is to have the pregnancy result in a full term, healthy, non-syphilitic infant and therapy is directed entirely toward this end. Save for a consideration of the mother's ability to tolerate treatment, the status of the infection in the mother is to be temporarily disregarded. It so happens in most cases that the appropriate treatment for the welfare of the infant is also singularly beneficial to the mother and may serve to arrest her infection. If, however, the method of treating effectively the mother's infection varies from that essential for the protection of the fetus, then treatment during pregnancy must be planned for the benefit of the expected offspring and proper care of the mother's infection be postponed until a full term, healthy infant is secured.

The principles of prenatal therapy are based upon these following

ideas:

1. The infection of the fetus occurs in the latter half of the pregnancy, but since the transplacental transfer may be delayed even to the time of delivery, it is never too late to begin therapy.

2. If the therapy is begun before the fifth month the arsenicals tend to clear the infection from the mother's body and also are stored in the placenta to form an effective barrier so that infection of the fetus does not occur.

3. If therapy is not begun until after the fifth month and if by this time the fetus has already been infected, then it is believed that the heavy metals and arsenicals pass the placental barrier in sufficient quantities to actually treat the infection within the fetus. However, the sooner the placenta can become impregnated with the spirillicidal drugs, the better are the chances for a healthy child. We must realize this is not the most effective means of therapy, but will prevent a continual feeding of spirochetes into the fetus from the mother and even though it may not cure the disease in the infant it will probably hold the infection in abeyance and prevent an overwhelming toxemia resulting in a stillbirth or grossly diseased child, so that we at least obtain a living treatable infant.

The drugs used in modern therapy of syphilis in the pregnant woman have essentially become limited to the trivalent arsenical compounds and the heavy metals of which bismuth and mercury are most used.

The trivalent arsenicals now in popular use include the following:

1. Arsphenamine. This drug is given in doses of 0.3 to 0.4 grams at weekly intervals.

2. Neoarsphenamine. This drug is usually administered weekly in doses of 0.45 to 0.6 grams.

3. Mapharsen. This drug is administered in doses of 0.04 to 0.06 grams and since it is more rapidly excreted than the aforementioned drugs, may be given at intervals of four to five days.

The heavy metals are used in so many different forms that it would be impossible to discuss the various compounds in this article. Suffice to say that bismuth is preferred by many men and the most common bismuth compounds used are:

1. Bismuth subsalicyate - suspended in oil, which is given in doses of 0.2 grams.

2. Potassium bismotartrate in doses of 0.2 gram.

3. Sodium bismuthate given orally in doses of 1.2 to 1.8 grams daily or intramuscularly.

There are a few men, however, of which Mc Cord is the most promi-

nent, who believe that mercurial inunction is better tolerated by the pregnant woman.

The schemes for the treatment of syphilis in various stages of pregnancy, as recommended by the United States Public Health Service, are as shown in the following chart. This chart contains the basis for therapy of pregnant syphilitic women which generally follows the schemes put forth by most modern syphilogists, however a few points of difference and additions as presented by different authorities will be discussed briefly later on.

CHART I

Week of Gestation	Treatment of syphilis discovered in the first trimester of pregnancy	Treatment of syphilis discovered in the second trimester of pregnancy	Week of Gestation	Treatment of of syphilis discovered in the first trimester of pregnancy	Treatment of syphilis discovered in the second trimester of pregnancy
	[1]				
1	Arsenical		21	Arsenical	Arsenical
2	Arsenical		22	Arsenical	Arsenical
3	Arsenical		23	Arsenical	Arsenical. Bismuth
4	Arsenical		24	Arsenical	Bismuth
5	Arsenical		25	Arsenical. Bismuth	Bismuth
6	Arsenical		26	Bismuth	Bismuth
7	Arsenical		27	Bismuth	Bismuth
8	Arsenical		28	Bismuth	Bismuth
9	Arsenical [2]		29	Bismuth	Bismuth
10	Arsenical. Bismuth		30	Bismuth	Bismuth
11	Bismuth		31	Bismuth	Arsenical
12	Bismuth		32	Arsenical	Arsenical
13	Bismuth		33	Arsenical	Arsenical
14	Bismuth	Arsenical	34	Arsenical	Arsenical
15	Bismuth	Arsenical	35	Arsenical	Arsenical
16	Bismuth	Arsenical	36	Arsenical	Arsenical
17	Bismuth	Arsenical	37	Arsenical	Arsenical
18	Arsenical	Arsenical	38	Arsenical	Arsenical
19	Arsenical	Arsenical	39	Arsenical	Arsenical
20	Arsenical	Arsenical	40	Arsenical	Arsenical

1. One of the trivalent arsenical compounds discussed on the previous page, used in the appropriate dosage.

2. One of the bismuth compounds used in the appropriate dosage.

There are a few points brought forth in Chart I which need to be emphasized:

1. Regardless of the time in pregnancy at which syphilis in the mother is discovered, her treatment from that point forward should contain a maximum of treatment with an arsenical.

2. Regardless of the duration of pregnancy at the time at which the infection in the mother is discovered, treatment should be so planned that she will receive an arsenical in full dose for at least six weeks before delivery.

3. In case the infection in the mother is discovered late in pregnancy, simultaneous treatment with arsenical and bismuth should be carried out.

When the treatment is begun early in pregnancy most syphilogists agree to the scheme of the United States Public Health Service, however a few feel that a combined method of treatment should be used. That is appropriate arsenical and heavy metal be given weekly for six to eight weeks, then four to six weeks on the heavy metal alone, and then combined therapy again for six to eight weeks and so on throughout the pregnancy, but always ending with the arsenical in the last four to six weeks before delivery. The Cooperative Clinical Studies in the Treatment of Syphilis as published through the United States Public Health Service have shown that the alternating method of therapy is more effective than the combined course of treatment, if treatment is started early.

There has also been some difference in opinion on the drugs that should be used. Most of the men recommend either arsphenamine or neoarsphenamine, but the use of mapharsen is becoming increasingly popular. Costallo has condemnedmapharsen and states that neoarsphenamine is the drug of choice. However, Minnich in a comparison study feels that mapharsen gives equally good results as neoarsphenamine and seems to be better tolerated. The Wisconsin State Board of Health for the greater part supplies mapharsen to the numerous syphilis clinics and report equally beneficial effects with this drug as with the other arsenicals. In the final analysis of this difference it may be said that the differences among the three arsenicals is small, and the important point is that the doctor use one of these drugs in its proper method and the results will be most gratifying.

The dosage of the different drugs has been given as the amount best tolerated and most effective in the average woman. Thus, no hard set rules may be set down as to the amount to be used, this must be left in part to the physician who must treat his patient. Some men feel that the initial doses should be smaller than those given and gradually built up to the full adult female dose. Stokes and Ingraham, for instance, recommend that the first dose of neoarsphenamine be 0.2 gram and gradually built up so that the average dose for the first three weeks does not exceed 0.3 gram and that the total weekly dose need never exceed 0.45 gram. Moore feels, however, that arsphenamine or neoarsphenamine may be given in 0.3 and 0.6 gram respectively right from the start. Minnich in his work with mapharsen found that 0.05 gram weekly dosage seems to be the most effective.

If syphilis is not discovered in the pregnant woman until after the sixth month, then the mother should receive weekly doses of an arsenical until delivery and combined with this six to eight weekly intramuscular injections of bismuth. Regardless of when syphilis is discovered in pregnant women, they should be given as many injections of arsenic as time will permit. Even if discovered near delivery, one or two injections may be of some benefit, especially if the mother has a primary lesion at the time, as they may prevent infection of the infant during its passage through the birth canal.

Cole states that even late inadequate therapy materially increases the possibility of a normal child.

Whether to treat a syphilitic woman during each pregnancy has long been a debatable issue. The Cooperative Clinical Group came to the conclusion that the woman should be treated during each pregnancy. Ingraham, however, has long held that this is an unwarranted and dangerous procedure. It seems that therapy is not warranted during every pregnancy providing the mother has had adequate treatment previously with a reversal of her Wassermann reaction. Hoffman has said that a new course of treatment is not necessary in later pregnancies in women who have been treated intensively and systematically and whose cure may be assumed with sufficient probability. However, it must be recognized that a certain percentage of these women will at subsequent pregnancies deliver syphilitic infants and it is upon the basis of these facts that many feel women should be treated during each pregnancy. Again, I should say the procedure carried out be governed by the individual physician who is called upon to

make the decision.

Probably no therapy is attended by such gratifying results as is that of adequate prenatal antisyphilitic treatment when we consider that about two-thirds of the pregnancies of syphilitic women end disastrously if no therapy is given them during the pregnancy. With adequate treatment about ninety to ninety-five per cent may deliver healthy nonsyphilitic offspring.

The results of antisyphilitic therapy of pregnant women from the Johns Hopkins Clinic are typical and will serve as an example of what can be accomplished:

CHART II

No treatment	54.1% Living 45.9% Dead	35.4% Normal Nonsyphilitic 64.5% Syphilitic
Arsphenamine less than 1 gram	89% Living 11% dead	75% Nonsyphilitic 27% Syphilitic
Arsphenamine 1 to 2 grams	90% Living 9.4% Dead	78.7% Nonsyphilitic 20.2% Syphilitic
Arsphenamine 2 to 3 grams	91.8% Living 8.2% Dead	83.8% Nonsyphilitic 16.1% Syphilitic
Arsphenamine 3 to 4 grams	100% Living 0% Dead	87.5% Nonsyphilitic 12.5% Syphilitic
Arsphenamine 4 to 5 grams	94.7% Living 5.3% Dead	100% Nonsyphilitic 0% Syphilitic

This means when adequate treatment, which has come to be regarded as ten or more treatments, is given the possibility of getting a living nonsyphilitic infant is between eighty-seven and one hundred per cent.

Cole reports similar figures and has shown that with adequate

treatment begun before the fifth month, the mother will have a living non-spyhilitic infant in ninety-one per cent of the cases. He further reports that in his series, if treatment was begun before the fifth month, 78.4 per cent of the children were living nonsyphilitic and only 6.6 per cent were syphilitic, not considering the amount of therapy. If the treatment was begun after the fifth month only 60.6 per cent of the children were living and nonsyphilitic and 23.4% were syphilitic. In those women with early syphilis, abortions or stillbirths occurred in 46 per cent of the cases when no treatment was given but in only 7.6 per cent of the cases when even small amounts of treatment were given late in the pregnancy.

Mc Cord states that only 5.4 per cent of the pregnancies end disastrously in patients receiving ten or more treatments, and women with no treatment gave birth to 57.6 per cent of the prematures, whereas those with adequate treatment accounted for only 7.1 per cent of the prematures. He adds that 87 per cent of the late abortions occurred in women with no treatment, where none occurred in the adequately treated group. Of the early abortions 84.6 per cent had no prenatal treatment and the number of early abortions decreased with increased antepartum treatment. This worker says, "Increasing experience leads me to believe that maternal syphilis is probably a more frequent cause of early abortion than is now believed." The Cooperative Clinical Group in their study of this problem found that 68 and 78 per cent of the women who previously had experienced two or three abortions respectively were able to bear living children after receiving antisyphilitic treatment.

Moore found the best results were obtained when treatment was

given both before and during pregnancy when 95.5 per cent had living non-syphilitic children, whereas if treated only before pregnancy 91.3 per cent had normal infants and if treated only during pregnancy 87.5 per cent had normal infants.

In summarizing the effects of therapy upon the outcome of the pregnancy, it may be said that if treatment is begun early and adequate treatment is given, the percentages of abortions and stillbirths will be very low and the chances for a living nonsyphilitic infant will be about 90 to 95 per cent.

COMPLICATIONS DUE TO ARSENICAL THERAPY

The question of the frequency and severity of arsenical reactions in pregnant syphilitic women has aroused a great deal of controversy, on the treatment of these women. The Cooperative Clinical Group showed that gastro-intestinal reactions are somewhat more frequent in pregnant women and kidney irritability was four times more frequent. Whereas the greater frequency of nitritoid reactions, pruritus and slight skin eruptions occurred in women never pregnant. Crustaceous dermatitis was twice as frequent in women never pregnant and icterus was more than five times as frequent in women never pregnant, as in pregnant women. This group, therefore, concluded that the pregnant syphilitic woman is a good risk for arsenical therapy and in most cases will stand her therapy better than the woman who never has been pregnant.

Ingraham, Plass and others have strenuously opposed this rational as in their experiences syphilitic pregnant women have reacted unfavorably

to arsenical therapy in some cases. Ingraham reported forty-two maternal deaths from arsenical reactions. In his report 64.3 per cent resulted from acute hemorrhagic encephalitis, 9.5 per cent from acute circulatory collapse, 7.1 per cent from parenchymatous degeneration of the liver and kidneys, 4.8 per cent from Crustaceous dermatitis, 2.4 per cent from aplastic anemia, 2.4 per cent from eclampsia resulting form antiluetic therapy and 9.5 per cent from unknown causes. Plass and Wood reported three cases of acute hemorrhagic encephalitis which resulted in maternal deaths. It should be brought out here that these three deaths occurred in women in the last trimester who were receiving two injections of arsenical a week.

Peckman, reviewing a series of 13,742 consecutive deliveries at Johns Hopkins Hospital, concluded that the incidence of toxemias of pregnancy was somewhat lower in syphilitics than in nonsyphilitic patients. The general incidence for the entire clinic being 18.21 per cent and in women receiving arsenical therapy during pregnancy 14.93 per cent.

In summarizing the discussion of this question it should be pointed out that:

1. Pregnant women cannot be treated with arsenicals without some small risk.

2. Pregnant women are more susceptible to acute hemorrhagic encephalitis, transient kidney and liver involvement and gastro-intestinal reactions.

3. The question of individual intolerance or idiosyncrasy

must be considered.

Therefor the physician must use care in the treatment of pregnant women and watch his patients carefully. Probably the safest method is to use some preparatory treatment before beginning arsenical therapy, especially in the latter half of the pregnancy and finally that the safest interval between injections of arsenicals in the latter half of pregnancy is not shorter than one week.

SUMMARY

In summary of this discussion I wish to bring out the following points:

1. The incidence of syphilis varies remarkably in this country, depending mainly on the percentage of negro and poor white population. However, the figures in general vary between 0.1 and 16.3 per cent.

2. We have come to know that syphilis effects the pregnant woman differently than the nonpregnant woman or male. The disease in general tends to be milder and runs a benign course to become latent in type.

3. If an untreated syphilitic woman is allowed to go to term, she has only about a 16 to 35 per cent chance of having a living nonsyphilitic child.

4. The fetus for all practical purposes is infected by way of the placenta, following the original infection in the mother with a subsequent spirochetemia sometime during her pregnancy. This infection does not occur until after the fourth to sixth month, after the protective Langhans layer has disappeared.

5. The diagnosis of syphilis in the pregnant woman is more frequently made if a blood serologic test is preformed routinely, along with a careful history and physical examination.

6. The diagnosis of syphilis in the infant may be best made by combining methods of diagnosis. The cord and blood Wassermanns early are not diagnostic, but suggest need for further study. The roentgenologic examination may early give the diagnosis, as may the examination of the placenta, cord scrapings and demonstration of organisms in the placenta. Finally, a pediatric follow-up may be necessary to establish the diagnosis.

7. The treatment of syphilis is best carried out by beginning it early in pregnancy, using alternating courses of an arsenical and heavy metals, and continuing throughout the pregnancy and ending the last six weeks with arsenical therapy.

8. If treatment is begun early and continued throughout the pregnancy, the mother has between an eighty-seven and ninety-five per cent chance of having a healthy nonsyphilitic infant. Even if treatment is not begun until late, a few injections of an arsenical will materially increase the chances for a normal child.

9. The pregnant woman is generally less susceptible to the severer complications of arsenical therapy than the nonpregnant, except for the acute hemorrhagic encephalitis. It may generally be said that with average care and good judgment the pregnant women may be safely treated with arsenicals.

CONCLUSION

Syphilis in the pregnant woman, although not extremely common in this part of the country, occurs often enough that it should be carefully looked for in every pregnant woman. I, therefore, recommend that the blood Wassermann be a routine procedure on every pregnant woman on her first prenatal visit. Thus, we begin her prenatal care with the diagnosis of the disease with which we have to deal throughout her pregnancy. The duty of the physician then remains to begin the therapy early and continue adequately throughout the pregnancy. The reward for the early recognition and adequate treatment will in the vast majority of cases be a full term healthy nonsyphilitic infant, which is the ultimate goal of every physician who cares for the pregnant mother.

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