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SYPHILIS
COMPLICATING
PREGNANCY



OUTLINE OF THESIS

Introduction.

Clinical Review of 152 cases.

1. Early syphilis complicating pregnancy
2. Latent or late syphilis complicating pregnancy
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INTRODUCTION

152 cases of syphilis complicating pregnancy are presented for review and discussion. These women attended the maternity department in the decade August 1942 to August 1952 during which time a revolutionary change in treatment took place (1945) with the introduction of penicillin as a powerful anti-spirochaetal agent.

A short commentary on this subject was prepared early in 1949 as part of the requirements for the examination for membership of the Royal College of Obstetricians and Gynaecologists. At this time, the subject was reviewed under 4 clinical groups. This clinical classification has been retained in the present thesis.

Classification and the numbers in each group are as follows:-

1. Early syphilis (primary or secondary) 37
2. Latent or late syphilis 65
3. Congenital syphilis 16
4. Previously fully treated acquired syphilis.. 34
undergoing prophylactic treatment during
pregnancy.

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CLINICAL REVIEW

of

152 CASES OF SYPHILIS COMPLICATING PREGNANCY

GROUP 1

Early acquired Syphilis 37 cases

Diagnosis.

In this group, the diagnosis can be quickly established by:-

- (a) History - exposures, time of appearance of lesions, last menstrual period, etc. It is to be noted that by taking the above into account, one can, not infrequently, assess that conception and infection occurred at the same time.
- (b) Clinical Examination - demonstration of primary and secondary lesions.
- (c) The demonstration by dark ground illumination of *Spirochaeta pallida* in the serum from primary or secondary lesions.

Of the 37 cases of early syphilis diagnosed during pregnancy or immediately after, the numbers in the primary and secondary stages were as follows:-

1) Primary	10
(a) Seronegative	1
(b) Seropositive	9
2) Secondary	27
		<hr/>
		37
		<hr/>

Batchelor (1) states that infection acquired during any stage of pregnancy is characterised by severe primary lesions owing to the local vascularity of the pelvis. Several of the above cases showed large primary lesions and in one case the primary measured 3" x 2". Most authorities mention that secondary lesions are often very slight but this is not a feature in this series as most of the 27 cases had well marked and widespread manifestations.

The Role of Serology in early acquired syphilis.

There is a common tendency (outside venereology departments) to regard the serological tests - Wassermann and Kahn or other similar tests - as the beginning and end of all syphilitic investig-

ation. These tests are of the utmost importance in the diagnosis of latent acquired syphilis. However, it must be emphasized that in the vast majority of cases in this group, the diagnosis can be made and treatment instituted before the result of the blood test is to hand.

By relying solely on positive serology valuable time is lost before treatment is commenced. It is a bad principle to base the diagnosis of syphilis on only one result. False positive results do occur although we have found no evidence that they are more common in pregnant women. Therefore serological tests must be repeated on one or two occasions at least before the diagnosis is made and treatment begun.

Furthermore, if routine serology is relied upon to the exclusion of clinical examination, there is danger of missing the diagnosis (at least temporarily and with possible unfortunate results particularly to the foetus) in cases of primary syphilis where the primary lesion has appeared with *Spirochaeta pallida* readily demonstrable but the serological tests have not yet become positive. The time between the appearance of the primary lesion and the positivity of the blood test is usually 2 to 4 weeks.

However, serological tests are of value in this group:-

- (a) Staging of Primary Syphilis (i.e. seronegative or seropositive)
- (b) Response of the disease to treatment in the follow-up period. The cases are followed up after treatment by quantitative Wassermann and Kahn tests at regular intervals - usually monthly - until delivery, and progress observed. Satisfactory response is denoted where the titre falls and the serology reverts to negative. Where the treatment was commenced before the 28th week most cases were negative in the later weeks of pregnancy and at delivery. Where the titre remains high or actually increases, the response to therapy may be taken as unsatisfactory and further treatment is indicated. Of course, titre serological estimation has been of particular value since the introduction of penicillin therapy because where there is unsatisfactory response, a further full course of penicillin treatment can be given in a matter of days. In 2 cases (one treated before 28 weeks: one treated after 28 weeks) the blood titre remained high and a second course of penicillin was given with effect. In some cases treated after 28 weeks, delivery occurred too soon after treatment to allow for satisfactory quantitative follow-up, the blood still being strongly positive at delivery.

TREATMENT.

During the period under discussion, great changes in the treatment of syphilis took place. Between 1942 and 1945 the pregnant woman was treated by intravenous arsenic and intramuscular bismuth injections. The dual injection was given for 10 consecutive weeks, the course consisting of 4.65 to 6.15 gms. of arsenic (depending on weight and general health) and 2.0 gms. of bismuth in divided dosages. Four weeks rest followed. The above course was then repeated the object being to give as much treatment as possible before delivery. This was the method employed in this series. No arsenic was given 2 - 4 weeks before term in order to avoid toxic reactions.

With the advent of penicillin, a new powerful anti-spirochaetal agent was introduced into the field of treatment and was being first used in this hospital in 1945. For a short time it was used alone, and then in conjunction with bismuth. The total course of penicillin was 2.4 mega-units initially. The penicillin was in aqueous solution, 40,000 units being given by intramuscular injections 3 hourly for 7½ days. The total dose was later increased to 4.8 mega-units. 10 weekly injections of 0.2gms Bismuth were given intramuscularly.

Penicillin in combination with arsenic and bismuth was the next method of treatment to be employed and at the time (1946-1948) was believed to form the strongest attack against the spirochaeta pallida. The rationale of treatment was that penicillin and arsenic had a short powerful effect, some authorities also believing that there was a synergistic action between them when used together. The bismuth exerted a slow steady influence on the organism.

During this period, the usual course of treatment was as follows:-

- Penicillin - 5 mega units (500,000 units in beeswax oil in a single daily intramuscular injection for 10 days.
- Arsenic - Neo-arsphenamine - trivalent.
10 weeks treatment given. In first week 2 injections, one of 0.3 gms and one of 0.45 gms were given intravenously and thereafter at 0.45 to 0.6 gms weekly.
- Bismuth - 10 weekly injections of 0.2 gms by intramuscular injection.

In this unit, arsenic and bismuth therapy was instituted at the same time as the penicillin course. However, it gradually became evident that results from clinics where penicillin alone had been used were as satisfactory as the results of penicillin-arsenic-bismuth regimes. Also some pregnant women are peculiarly sensitive

to arsenic therapy and death is a recognised risk .. being due to encephalopathy: also purpura, dermatitis and jaundice. Bismuth has also toxic properties, particularly as a kidney irritant. In view of the two above factors, penicillin has been used alone since early 1949. The total dose has been increased and a course of 10 mega-units is now given - 1 mega unit of penicillin in beeswax oil being given intramuscularly in a single daily injection for 10 days.

Penicillin in beeswax oil allows for slow absorption and only 1 daily injection is given, this maintaining a satisfactory blood level over 24 hours. It has allowed patients to be treated as out-patients whereas previously with aqueous penicillin all cases were admitted to hospital. Patients are now admitted for treatment only when there is severe local reaction (e.g. marked secondary infection of the primary lesion) or on account of bad social conditions or other obstetrical factors.

Number treated by each method:

1) Arsenic and bismuth	8
2) Penicillin	
a) Alone	8
b) with arsenic and bismuth..	11
c) with bismuth	4
No treatment before delivery ...	<u>6</u>
	<u>37</u>

Results of Treatment.

(1) In cases diagnosed before 28th week of pregnancy.

	Seen at (Wks)	W.R. at 1st Visit	Stage of Disease	Treatment	W.R. at Del. ^{IV}	Del. ^{IV} at (Wks)	Fate	Follow-up
1.	12	++++	Secondary	As: Bis:	-ve	37	6/12 -ve	2 years -ve
2.	8	++	Primary	As: Bis:	-ve	39	6/52 -ve	2 years -ve
3.	25	++	Secondary	As: Bis:	-ve	40	Gd. Bld -ve	2 + years -ve
4.	20	+to++	Primary	As: Bis:	-ve	40	3/52 -ve	4/12 -ve
5.	17	++++	Primary	As: Bis:	++++		Aborted at 25 weeks	
6.	12	++++	late Secondary	Pen: Bis:	+++	38	8/52 -ve	2 years -ve
7.	16-18	-ve	Primary	Pen: Bis:	-ve	40	4/52 -ve	1 year -ve
8.	18	++++	Secondary	Pen: Bis:	-ve	40	5/52 -ve	16/12 -ve
9.	16-18	+++	Secondary	Pen: As: Bis:	-ve	40	6/52 -ve	2 years -ve
10.	12-14	++++	Secondary	Pen: As: Bis:	-ve	38	6/52 -ve	1½ years -ve
11.	12-14	++	Primary	Pen: As: Bis:	-ve	40	-ve at birth	1 year -ve
12.	20	++++	Secondary	Pen: As: Bis:	-ve	40	4/52 -ve	2 years -ve
13.	26	+++	Primary	Pen: As: Bis:	-ve	39	5/52 -ve	7/12 -ve
14.	12	++++	Secondary	Pen: As: Bis:	-ve	40	-- Default --	
15.	10	++	Secondary	Pen: As: Bis:	-ve	38	-ve at birth	2 years -ve
16.	16	++++	Secondary	Pen: As: Bis:	-ve	39	-ve at birth	2 years -ve
17.	18	+++	Secondary	(10)Penicillin	-ve	40+	-ve at birth	3 years -ve
18.	22	++++	Secondary	(10)Penicillin	-ve	40	-ve at birth	15/12 -ve
19.	16	++++	Secondary	(10)Penicillin	-ve	40	-ve at birth	1 year -ve
20.	14	++	Secondary	(9) Penicillin	-ve	40	-ve at birth	1 year -ve

Summary of Main Points.

- 1) Good results:- 19 infants were born alive and healthy, there being no stillbirths, neo-natal deaths, nor deaths in early infancy. There was one case of abortion at 25 weeks. The follow-up was satisfactory on the whole, and only one infant was not seen after discharge from hospital.
- 2) Diagnosis and Treatment. In the 20 cases there were:-

Primary syphilis -	
Sero-negative	- 1
Sero-positive	- 5
Secondary syphilis	- <u>14</u>
Total	- <u>20</u>

These cases were diagnosed between the 8th and 26th weeks of pregnancy and treated as follows:-

Arsenic and bismuth	-	5
Penicillin		
(a) alone	-	4
(b) with bismuth	-	3
(c) with arsenic and bismuth	-	<u>8</u>
Total	-	<u>20</u>

3) Serology.

a) Maternal.

In 17 cases out of 20 the Wassermann and Kahn tests were negative before delivery, one being primary sero-negative at time of diagnosis and remaining in this state throughout.

In 2 the blood tests remained positive, one (case 5) being strongly positive when abortion occurred at the 25th week. No actual proof as to the cause of abortion was obtained but late abortion is a feature of syphilis complicating early pregnancy and so the disease may well have caused this abortion.

In the other (case 12) the blood was still positive at delivery but in diminished titre, a second course of 5 m.us. of penicillin having been given with effect.

In the last case the serology was +++ at delivery.

b) Infant.

At one time, no blood tests were taken as a positivity did not necessarily indicate syphilis but might be due to

maternal antibodies passed via placenta into the foetal circulation. The practice was to bring the infant back at the 6th week of life and assess. This was the method generally carried out earlier in the series. It is seen that all the bloods examined between 4-8 weeks were negative. However, cord blood and venous blood by heel stab are now taken at time of delivery in every case. The reason for this is discussed later.

2) Treatment after 28th week of pregnancy

	Seen at (Wks)	W.R. at 1st visit	Stage of Disease	Treatment	W.R. at Delivery	Delivery at (Wks)	Fate	Follow-up
1.	32	+++	Primary	As:Bis	+++	40	S.B.-C.S.(PM)	-
2.	30-2	+++	Secondary	As:Bis.	+++	38	Died at 6/52 Br-pneumonia	-
3.	30	++++	Secondary	As:Bis.	++	39	seen at 3/12 WR+++	Default untreated
4.	28	++++	Secondary	(.6) Penicillin	++++	30	S.B.-macerated foetus.	-
5.	30	++++	Secondary	(3) Penicillin	+++	34-6	Died at 3/52 C.S. p.m.changes	-
6.	34	++	Secondary	(8) Penicillin	-ve	40	cord blood - ve - ve at 6/52	1 year -ve
7.	30	++	Secondary	Pen:As:Bis	+	38	cord blood -ve at 6/52	2 years -ve
8.	34	++++	Secondary	Pen:As:Bis	++++	40	Died at 5/52 gastro-enteritis	-
9.	28	+++	Secondary	Pen:As:Bis	+	41	-ve at 6/52	2 years -ve
10.	34	++++	Secondary	Pen:As:Bis	+	38-40	-ve at 6/52	18/12 -ve
11.	28	++++	Secondary	Pen:Bis.	++++	34	Stillbirth	-

(1) Results. The results in this group give cause for consideration as only 4 out of 11 survived and were in good health at 1 to 2 years after birth

- 1) Intrauterine death - 3 (2 changes due to congenital syphilis
(- liver spleen, and
(placenta showed syphilitic changes
(
(1 - no post mortem carried out.
- 2) Died between 3 & 6 weeks - 3. (a) 3/52. congenital syphilis -
post mortem syphilitic
changes.

(b) 6/52. broncho-pneumonia -
post mortem - lungs only
examined. No special
investigations for
congenital syphilis.

(c) 5/52. Gastro-enteritis.
No post mortem.
- 3) Congenital syphilis - 1. Wasserman reaction +++ at 3/12.
Default. Not treated.
- 4) Alive and apparently well - 4. Follow-up 1-2 years
(negative Wassermann)

No anti-syphilitic treatment given to any babies.

2. There were 4 cases of proved congenital syphilis in this group.

2 intra-uterine death PM.Histology - CS.

1 neo-natal death at 3 weeks (clinically) PM.Histology - CS.

1 case of congenital syphilis at 3 months - defaulted; no
treatment.

3. 6 deaths occurred 3 intra-uterine deaths
3 within the first 6 weeks of life.

2 intra-uterine deaths were due to syphilis and no P.M. was carried
out in the 3rd.

Study of the obstetrical case records revealed no obstetrical
cause such as toxæmia, ante partum hæmorrhage, congenital
abnormalities which might have accounted for intra-uterine death.
1 infant died within 3 weeks from proven C.S. the liver and spleen
showing syphilitic change. The two others died of broncho-
pneumonia and gastro enteritis at 6 and 5 weeks respectively.

No post mortem was carried out in the latter. In the former case, the child was admitted to hospital with severe broncho-pneumonia. No mention was made in the medical notes that the mother had been treated for syphilis in pregnancy. In the P.M. request, there was similarly no note made of this fact and so no search was made for C.S. (e.g. liver spleen bones). There was only a histological section of lung available for study and in the section only an overwhelming infection with little lung tissue was seen.

The point to emphasize from these 2 cases is that with the history of maternal syphilitic treatment late in pregnancy these children may have suffered from congenital syphilis which resulted in poor general condition and the respective acute infection supervened as the terminal factor. These two deaths may therefore have been due primarily to untreated congenital syphilitic. One cannot say, however, but every case should be very closely followed up and investigated. Such good results are being reported by American authorities that where one has only 4 infants out of 11 alive and well, critical survey of causes is required.

4. Treatment by Arsenic & Bismuth.

Of the 3 cases treated by arsenic and bismuth, one died in utero, one died at 6 weeks and one was known to have congenital syphilis at 3 months. These results are poor but most authorities agree that arsenic and bismuth used late in pregnancy was not satisfactory.

5. Treatment by Penicillin, (either alone or combined with arsenic and bismuth).

Penicillin is now the main anti-syphilitic agent and so the results from this treatment must be considered. 8 cases are available for study.

4 were alive and well at 1 to 2 years
-ve serology

2 intra uterine deaths occurred - one woman having had only 0.6 mega units penicillin a macerated foetus being passed during treatment. The other received 4 mega units penicillin and bismuth and went into labour 4 weeks after treatment. The foetal heart was heard 1 week before delivery. No P.M. was carried out.

2 infants died within 6 weeks ... one of congenital syphilis (proven) and one of gastro-enteritis (vide supra)

Earle Moore (2) states - if mothers with primary or secondary syphilis were treated with penicillin, the morbidity and mortality in infants was reduced to somewhere between 1 and 2%,

indicating that it had been possible to reduce the incidence of congenital syphilis almost to vanishing point The results were equally good when the mothers were treated late.

8 cases of early syphilis treated late in pregnancy form a small series but any one individual is not likely to see to-day a great number of such cases.

In these 4 cases, one foetus had probably been overwhelmed and was on the point of dying in utero when penicillin was commenced, so, in fairness, one can't say the therapeutic agent failed in this case. The other three, adequate penicillin therapy having been given at least 4-6 weeks before delivery may well have died as a result of congenital syphilis. One is definitely known to have done so and there was insufficient investigation in the others to establish the primary cause of death.

I agree that the results when treatment is instituted before 28 weeks are very satisfactory. However, it would appear from this series that when the treatment is delayed until after 28 weeks the results are not good. I feel that further study is necessary in this latter group and would advise extreme vigilance when dealing with such cases - individual successful cases obviously do occur as can be seen in this series. At the same time one should also bear in mind the failures and possible failures and thus try to keep the problem in perspective.

One important point is that in successful cases, the maternal serology had reverted to negative or the titre was diminished at delivery, while in the 4 cases associated with stillborn infants or death early in life, the blood tests were strongly positive at delivery. This may possibly be of some value in prognosis for the infant if born alive.

6. Previous ante-natal care.

7 cases had had no previous ante-natal care - 3 being referred to the V.D. department on account of the signs, and 4 reporting to the ante-natal clinic first. 4 cases had been under ante-natal care but in no case had blood been taken for routine Wassermann and Kahn by the practitioner.

- (3) Early Acquired Syphilis. Diagnosed at delivery or in the puerperium.
No treatment given.

First seen	Stage	Treatment (ante-natal)	W.R. at Del ^{ry} .	Delivery at	Fate	Follow-up
1. In labour	Primary	Nil	++	40	6/52-Con.Syph. Rash.Sp.pall+	Treated -ve at 2 yrs
2. In labour	Primary	Nil	++++	40	-ve at 6/52	Default
3. In labour	Primary	Nil	++++	38	- Default	-
4. In labour	Secondary	Nil	+++	36	Died 16 days. CS-p.m.changes	
5. In labour	Secondary	Nil	++++	34	Died 24 hrs. C.S.changes	
6. In labour	Secondary	Nil	++++	38	- Default	-

(1) Results.

- | | |
|------------------------------|---|
| 1) Neo-natal Deaths | 2. P.m.changes of congenital syphilis. |
| 2) Congenital syphilis | 1. Clinical evidence of congenital syphilis. Treated - ve at 2 years. |
| 3) Fate unknown | 3. One - ve 6/52 default thereafter. Two not seen after hospital discharge - no Venous or cord blood taken. |

The results in this group are therefore highly unsatisfactory: 3 cases of known congenital syphilis, there being 2 neo-natal deaths. One died 24 hours after birth before the maternal diagnosis was made. The other commenced treatment on the 5th day having 150,000 units penicillin daily but death occurred on the 16th day. The remaining three defaulted, two immediately after discharge from hospital and one after the 6th week at which time the baby's blood was negative. The fate of these three is unknown.

- (2) In the 3 cases of primary syphilis, the disease was acquired in

the later stages of pregnancy probably between the 32nd and 36th weeks.

In two of the cases of secondary syphilis, the infection was probably acquired at or shortly after conception as a primary sore was noted in each case at roughly the third month of pregnancy. In the remaining case, a healed primary was seen but no actual date of infection was obtained.

(3) Previous Ante-natal Care.

5 were admitted mainly on social grounds having had no ante-natal care or made any arrangements for delivery. Thus, it is scarcely surprising that 3 defaulted on discharge. The infants of the remaining two died neo-natally.

The 6th case (No.1 in previous table) is of some interest. She attended the hospital ante-natal clinic throughout pregnancy, the routine Wassermann and Kahn tests at the first visit being negative. No lesion was noted in the later weeks, the primary being discovered early in puerperium. The infant developed congenital syphilis but responded well to treatment. Some authorities, Murrell⁽³⁾, Heyman & McCain⁽⁴⁾, advise routine blood test at 36 weeks as well as the first visit. Thus, the occasional case, such as this one, may be discovered and treatment given before delivery with better prospect for the infant.

GROUP 2

Latent Syphilis Complicating Pregnancy 65 cases

Investigation and Diagnosis.

The cases in this group are discovered typically as a result of positive routine Wassermann and Kahn tests.

When a positive blood test is obtained from an ante-natal patient, an immediate appointment should be made for her to return to the ante-natal or V.D. clinic. It is important that further investigations should be carried out - and treatment instituted if necessary - as soon as possible. I have seen several cases in the earlier months of pregnancy where the routine serological test at the first ante-natal visit was positive. The laboratory report had been attached to the patient's case sheet and nothing further done until the patient reported one month later. Valuable time was therefore lost. The patient could have been fully investigated in this time and if syphilis were confirmed, treatment commenced. Also, if the patient were about 4 to 5 months pregnant at her first visit, then in the lapse of one month the untreated syphilitic infection could have led to abortion. Therefore, all the results of laboratory tests should be seen by the medical officer or sister-in-charge of the ante-natal clinic, and if any test is positive, immediate action should be taken.

When such a patient reports, the following further investigations are carried out (preferably by a venereologist):-

1) Repeat serological tests - Wassermann, Kahn.

Syphilis should not be diagnosed on one positive result and the serological tests should be repeated on one or two occasions. I would say that it is advisable to have three consecutive strongly positive tests (both Wassermann and Kahn) before making a diagnosis of syphilis on serology alone. It is important to remember that false positive results occur and therefore error due to this should be avoided by repeating the tests. If the patient is seen very late in pregnancy, the time factor may not allow waiting for 3 tests, but history, examination of husband and clinical picture may help to confirm. I have known obstetrical colleagues inform a patient on the result of only one positive test that she had syphilis. Further investigations in the V.D. department were all negative but until this was proved, the patient passed through a period of much anxiety and misery. I would say that the word syphilis should not be used until the diagnosis has been definitely confirmed.

2) Careful history which includes enquiry into previous sores,

skin rashes, adenitis (inguinal and generalised) and sore throats. Family history - for evidence of congenital syphilis - is taken (see also page 29). The obstetrical history with details of previous pregnancies and children will have been already obtained. If a diagnosis of syphilis is definitely made, then history of exposures and contacts can be investigated - also arrangements made to examine husband (or consort, if known) and other children, if any.

3) Clinical examination with special regard to:-

- a) Healed early lesions.
- b) Late syphilitic lesions.
- c) Cardiovascular and central nervous systems; if involvement of either of these systems is suspected clinically, then an X-ray of chest or a lumbar puncture should be carried out (lumbar puncture is a difficult procedure to perform in late pregnancy and in such cases is better done after delivery).
- d) Signs of congenital syphilis - which may be minimal.

4) Differentiation between latent syphilis and congenital syphilis.

It is most important to distinguish between these two types as the outlook for the child is very different in the latter, third generation syphilis being exceedingly rare. If obvious congenital stigmata are present, the diagnosis is not difficult but some cases are without clinical signs and family history may be negative or impossible to obtain.

By careful attention to the details in paragraphs 2 and 3, it is often possible to obtain data which supports a diagnosis of latent acquired syphilis.

In the 59 cases of latent syphilis treated in the antenatal period, the following information was obtained:-

a) History of previous infection	15
b) Previous late abortions, stillbirths congenital syphilitic children	6
c) Husbands or consorts known to be syphilitic	9
d) Healed early lesions	6
e) Tertiary lesions present	2

It is often stated that one rarely finds a history of previous infection in these cases. In this series, however, it was found that 15 out of 58 gave such a history. My impression is that this number could have been increased. In some cases where initially no history was obtained, I found that after the patient had attended several times and gained confidence, a history of previous infection was obtained on further questioning. This further questioning was not always carried out and, in fact, from scrutinising certain case records, it would appear that little or no attempt had been made at any time to elicit such information.

However, should no significant history (personal or family) be obtained and no clinical signs present, it is safer to regard the case as one of latent acquired syphilis rather than congenital.

TREATMENT

Treatment followed roughly the same evolution as in early syphilis.

Combined arsenic and bismuth therapy was employed in the treatment of latent syphilis complicating pregnancy until early 1945. At this time penicillin was introduced into the field of antisyphilitic treatment. It was used alone in one or two cases but penicillin and bismuth soon became established as the treatment of choice in latent syphilis.

The penicillin-arsenic-bismuth regime was not favoured and used in only a few cases. If it had been intended to give neoarsphenamine, then a lumbar puncture would have been necessary (in latent syphilis) to exclude non-clinical central nervous system involvement. These patients tolerate trivalent arsenic badly. It was preferred not to subject the pregnant woman to lumbar puncture and as penicillin and bismuth proved very satisfactory, arsenic was omitted.

The penicillin course quickly increased from 2.4 to 4.8 mega units, some cases receiving a second course of penicillin. The bismuth course was the usual 10 weekly intramuscular injections each of 0.2 gm.

Since 1949, penicillin in beeswax oil has been used alone with equally good results, the total course now being in the region of 10 mega units.

In latent or late syphilis, severe Herxheimer reactions have been described when treatment is commenced with penicillin. McElligot(6)

states - "because of it's very powerful anti-spirochaetal action, penicillin should rarely be used initially without an adequate period of premedication with Bismuth. I have yet to see any Herxheimer reactions with these precautions. An exception to this rule can be made in the case of a young pregnant woman with negative findings on physical examination. In her case it is imperative that penicillin be given as soon as possible to ensure against her transmitting infection to her offspring." This is in agreement with the policy followed in this hospital.

Numbers treated by various methods:-

1) Arsenic and bismuth	7
2) Penicillin - a) with arsenic & bismuth	4
b) with bismuth	17
c) alone	<u>30</u>
	58
No treatment ante-natally -	<u>7</u>
	<u>65</u>

	Seen at (Wks)	Age & Status	W.R. (initially)	Treatment	W.R. at Delivery	Delivery at (Wks)	Fate	Follow-up	Previous Pregnancies.
1.	20	35 m	++++	As: Bis:	++++	40	-ve at 5/52	2 years -ve	1) 6 years -ve 2) S.B. 2 years ago.
2.	20	28 m	++++	As: Bis:	++++	40	-ve at 6/52	3 years -ve	1st pregnancy
3.	16	29 m	++++	As: Bis:	++++	37	-ve at 6/52	3/12-ve <u>Default</u>	1st pregnancy
4.	22	36 m	++++	As: Bis:	++++	32	Stillbirth	-	1) 13 years -ve 2) 3 years -ve
5.	12-14	37 m	++++	10 Pen:As:Bis:	++++	42	-ve at 8/52	<u>Default</u>	11 years -ve
6.	22	27 d	++++	4 Pen:As:Bis:	++++	40	-ve at 10/52	v.15 <u>Default</u>	1) 4 years -ve 2) N.N.D. 4th day
7.	18	32 m	++++	5 Pen:As:Bis:	++++	40	- Default	-	7 years -ve
8.	12	36 m	++++	5 Pen:Bis:	++++	38	-ve at 6/52	2 years	Abortion at 6/12
9.	16	37 m	++++	5.0 Pen:Bis:	++++	40	W.R. +++ 7.10.12 wks.	4/12 <u>Default</u>	4 infants - all -ve: last 5 years
10.	14	38 m	++++	4.8 Pen:Bis:	++++	39	Cord Bl+ve.-ve at 6/52	-ve 2 years	9 years -ve
11.	22-4	33 m	+++	4.8 Pen:Bis:	++	40	-ve at 6/52	2 years -ve	1st pregnancy
12.	14	36 m	++++	4.8 Pen:Bis:	++++	40	-ve at 4/12	<u>Default</u>	2) 8 & 6 yrs. -ve
13.	18	35 d	++++	2 Pen:Bis:	++++	38	- Default	-	1st pregnancy
14.	24	42 d	++++	2.4 Pen:Bis:	++++	40	- Default	-	Abortion at 5/12
15.	8	24 m	++++	- Pen:Bis:	++++	40	-ve at birth	18/12 -ve	1st pregnancy
16.	16	28 d	++++	5 Pen:Bis:	++++	38+	Cord Bl ++	<u>Default</u>	1) 5 years -ve
17.	14-16	35 m	++++	9 Pen:Bis:	+++	26+	Aborted at	26 /52 -	1) 6 years -ve 2) 2 years -ve
18.	11	34 m	++++	10 Pen:Bis:	++++	40	-ve birth	21/12 -ve	1) and 2) well. 3) died 11 days 4) died 28 days
19.	20	25 m	++++	6 Pen:Bis:	++++	36	-ve birth	1 year -ve	1st pregnancy
20.	14	37 d	++++	5 Pen:Bis:	++++	38	- Default	-	2 children.No tests.
21.	14	23 m	++++	5 Penicillin	++++	40	-ve at 4/52	2 years -ve	1st pregnancy
22.	20	24 S	+++	5 Penicillin	±	41	Cd.Blood -ve	3/12: <u>Default</u>	2 years: no test
23.	18	30 m	++++	10 Penicillin	++	39	Cd.Blood++ .-ve at 6/52	2 years -ve	1st pregnancy.
24.	16	32 S	++++	10 Penicillin	+++	40+	-ve at birth and 6/52	9/12 -ve	4 years -ve.
25.	16	27 m	++++	8 Penicillin	++++	38	-ve at birth and 6/52	2 years -ve	1st pregnancy
26.	18-20	23 m	++++	4.5 Penicillin	-ve	41	-ve at birth	18/12 -ve	1st pregnancy
27.	20	21 m	++++	10 Penicillin	++++	40	-ve at 2/12	to date 3/12	1st pregnancy
28.	16	26 m	++++	6 Penicillin	++++	39	C.S.at 4/12	treated	1st pregnancy
29.	24	34 m	++++	6 Penicillin	++++	38	-ve at birth and 6/52	4/12 to date	1) 10 -ve. 2) 12 -ve.
30.	26	28 m	++++	8 Penicillin	+++	40	-ve at birth - 6/52	18/12 -ve	1st pregnancy
31.	16-18	24 m	++++	10 Penicillin	±	40+	-ve at birth	4/12 -ve to date	1st pregnancy
32.	20	24 m	++++	10 Penicillin	++++	38-	-ve at birth	4/12 -ve to date	1st pregnancy
33.	12	21 m	++++	10 Penicillin	+++	40	-ve at birth	3/12 <u>Default</u>	1st pregnancy
34.	16	25 m	++++	10 Penicillin	++++	40	-ve at birth	6/12 to date	1st pregnancy
35.	24	25 m	++++	10 Penicillin	++++	39	-ve at birth	6/12 to date	1st pregnancy
36.	18	32 m	++++	12 Penicillin	++++	40	+ at birth and 1/12	18/12 -ve	1st pregnancy
37.	8	24 m	++++	6 Penicillin	++	41	-ve at birth	8/12 to date	1 Abortion 24/52
38.	22	42 m	++++	10 Penicillin	++++	40	- Default	-	1st pregnancy

1. Results.

In this group there were 4 unsatisfactory outcomes in a total of 38 pregnancies:

- 1) Late abortion at 26 weeks
- 2) Stillborn infant at 32 weeks
- 3) Congenital syphilis ... the infants WR and Kahn were strongly positive at 7 and 12 weeks.
- 4) Congenital syphilis ... the infant was admitted to hospital with congenital syphilis at 4 months of age.

- 1) In the case of the late abortion, syphilis as the cause was neither proved nor disproved. No histo-pathological examination was made. But in view of the time of abortion it is quite likely that syphilis was the actual cause.
- 2) The stillborn infant did show congenital syphilitic changes at post mortem. In this case treatment (arsenic and bismuth) was inadequate, the patient not attending regularly.
- 3) Congenital syphilis: in this case the mother was seen at 16 weeks. 5 mega units of penicillin with a total of 2.0 gms of bismuth were given. At follow-up, the WR and Kahn were still strongly positive at 12 weeks, the titre not diminishing. This infant was treated with penicillin. Default occurred at 4 months after birth.
- 4) The other case of congenital syphilis is of extreme interest and importance. The expectant mother was treated with 6 mega units penicillin when $4\frac{1}{2}$ to 5 months pregnant. In the case record is an entry after completion of treatment that a normal healthy infant could be anticipated. The delivery was normal and the infant looked healthy enough on discharge from hospital. No blood was taken for serological tests at birth. There was lapse in follow-up but at 4 months the infant was admitted to the children's ward suffering from the clinical manifestations of congenital syphilis. The WR and Kahn were both strongly positive.

It is generally stated that provided the syphilitic pregnant woman is treated early in pregnancy, a normal healthy infant (i.e. free from syphilis) can be expected. From the results in early syphilis treated early in pregnancy I would

say this is correct. But I find the above results disappointing and a source of some anxiety - there have been 2 cases of congenital syphilis, in both cases the mothers receiving what can be considered at the present time adequate treatment. In the case of late abortion which might well have been due to syphilis, the mother had also received adequate treatment, 8 weeks prior to abortion.

The results presented give the lowest possible incidence of congenital syphilis. The figure might even be higher because -

- a) 7 cases are still under surveillance - most being in the 1st 3 to 6/12 of their follow-up.
- b) 13 cases have defaulted
 - (i) 6 cases were negative between 2 and 4 months and default occurred thereafter. Two of these cases refused to attend initially for follow-up but after repeated letters and almoners visits were finally seen with the infants at 4 months. The infants were then negative. If these infants had been syphilitic, anything might have happened to them in these 4 months. Default then recurred. Also it is known that babies may become positive as long as 6-12 months after birth.
 - (ii) 6 cases were never seen again after discharge from hospital. In one, the serology was positive at birth. In the others no blood tests had been carried out or no record was discovered.
 - (iii) 1 case was negative at 10 weeks. A V.15 was given at this time but on contacting the clinic she was going to attend, there was no trace of her in the records.

It is possible therefore that the actual incidence of congenital syphilis in this group is higher than the figure given.

2. Prevention of Syphilis in this Group.

The question of preventing such cases of congenital syphilis occurring in this group arises.

Three courses which could be adopted suggest themselves:

- (a) The total dose of penicillin given in the initial course may be increased. As stated earlier, this has been increased and the usual course is in the region of 10 mega units. The two cases who had syphilitic children and the

case of late abortion received 5, 6 and 9 mega-units respectively. I doubt if the addition of a few extra mega-units of penicillin alone could be guaranteed to produce more effective results.

(b) Penicillin, combined with Metallic Therapy - i.e. bismuth with or without arsenic.

In this method, the penicillin would produce an immediate and powerful effect on the disease. The introduction of a 10 week course of bismuth would exert a slow continuous effect over this period on any *Sp.pallida* remaining after the initial course of penicillin. The disadvantages of these metallic agents in pregnancy have already been mentioned. Many authorities consider these unnecessary, their results being equally satisfactory without their employment. I also doubt if the re-introduction of these agents, used earlier in this series is the answer. It is to be noted that the mother of one of the syphilitic children and the patient who had the late abortion both had bismuth therapy, the former receiving a total of 2.0 gms over 10 weeks.

(c) A Second Course of Penicillin later in Pregnancy.

Most American authorities claim that retreatment is unnecessary and Goodwin (8) states that further therapy is only necessary should response to treatment be unsatisfactory. The only method of assessing response in this type of case is by serology - very few show late clinical manifestations in the age group under discussion. In cases of latent syphilis the Wassermann and Kahn reactions are often very difficult to reverse. This is most likely to happen where the disease is in the early latent stage (1 year or thereabouts). This was the stage in a few of the cases in this series (as can be seen in the foregoing table), the serology being negative at birth or positive in greatly diminished titre. But in the majority of cases, delivered 4 or 5 months after treatment, the Wassermann and Kahn reactions were as strongly positive as at the start of treatment. Therefore it is very difficult to assess the response to treatment in these cases.

I would suggest that where the blood is still strongly positive at the 32nd to 34th week of pregnancy, a second full course of penicillin should be given at this time in an effort to prevent the cases of congenital syphilis which sometimes occur where the mother has received a full course of penicillin early in pregnancy. A course of procaine penicillin 1 mega-unit daily for 10 days could be given, or a course of aqueous crystalline penicillin 500,000 units twice daily for 10 days to raise the tissue level to the highest degree.

3. Previous Pregnancies.

The number of previous pregnancies was 31 and the following information regarding them was elicited:-

a) Children tested and serology negative	21
b) Alive but not seen	3
c) Late abortions (5/12, 6/12, 6/12)	3
d) Stillbirth	1
e) Died - at 4, 11, 28 days respectively	<u>3</u>
		<u>31</u>

The exact cause was not known in any of the 7 unsuccessful outcomes. However, syphilis complicating pregnancy can cause late abortion, stillbirth and neo-natal death. It may well be that it was the cause in some or even all of these cases.

In latent syphilis, the history of previous pregnancies is of value for 3 reasons:-

- a) May help to distinguish between latent syphilis and congenital syphilis.
- b) May help in giving approximate duration of the disease. This is well illustrated in case 5 of table dealing with untreated latent syphilis in pregnancy. H/27

Para. 9	...	WR ++++	Kahn ++++
Pregnancies 1 to 6	...	normal 6th ... 5 years old. (children alive: last 2 - negative serology)
7	...	N.N.D. at 3 weeks	... 3 years previously.
8	...	abortion at 24 weeks 18 months ago.
9	...	current pregnancy	... stillborn infant ... 35 weeks - congenital syphilis.

From the above history, the suggested date of infection would be somewhere between $3\frac{1}{2}$ to 5 years previously. This is further supported in this case for it is known from the special clinic

records that this woman's husband was treated for secondary syphilis at the department about 4 years ago.

It is often quoted that syphilis acquired less than 4 or 5 years before the onset of pregnancy is a source of great danger to the foetus, its chances of becoming infected being very great. If the disease is of longer standing, then the foetus might escape. However, I think most would consider this to be of academic interest and that syphilis in complicating pregnancy would always be fully treated irrespective of time of contracting the disease.

- c) Bad obstetrical history (late abortions, stillbirths, neo-natal deaths in previous pregnancies) together with diagnosis of syphilis in current pregnancy would suggest syphilis as quite a likely cause of the previous unsatisfactory outcomes (e.g. the case quoted immediately above).

4. As points of general interest I have included:-

- | | | |
|----------------------------|-------|-----------------------------|
| a) Social status | | 31 married (m) |
| | | 5 divorced or separated (d) |
| | | 2 single (s) |
| b) The age of each patient | | |
| 12 out of 38 | | 35 years or more |

(2) Treated after the 28th week of pregnancy

	Seen at (Wks)	Age & Status	W.R. (initially)	Treatment	W.R. at Delivery	Delivery at (Wks)	Fate	Follow-up	Previous Pregnancies
1.	34	24 m	++++	As;Bis:	++++	40	-ve at 6/52	Default	1st pregnancy
2.	32	31 m	++++	As;Bis:	++++	40	-ve at 4/12	Default	1) 7 years -ve 2) 3 years. CS(I.K.)
3.	32-4	33 S	++++	As;Bis:	++++	40-	Stillbirth (no P.M.)	- -	1st pregnancy
4.	34	29 m	++++	Pen:As;Bis:	++++	40	± cord blood	Default	1st pregnancy (Blood donor!)
5.	38	27 S	++++	6 Pen;Bis:	++++	40	WR+++ 8/52 C.S.	Treated -ve at 6/12 Dft.	1) died at 2/12 ? cause
6.	36	33 m	++++	5 Pen;Bis:	++++	38	at birth +++ C.S.	Treated -ve 4/12: Dft.	1st pregnancy
7.	30	39 m	++++	5 Pen;Bis:	++++	40	at birth: 3/12 +++ C.S.	Treated - -ve 2 yrs.	1st pregnancy
8.	28	22 m	++++	2.4 Pen;Bis:	++++	39	-ve at 6/12	Default	1) 4 years -ve
9.	38-9	24 S	++++	3 Penicillin	++++	40	-ve at 3/52	Default	1st pregnancy
10.	34-6	37 S	++++	2.4 Penicillin	++++	41	- Default	-	1st pregnancy
11.	35	24 S	++++	3 Penicillin	++++	37	++ at birth (not treated)	Default	1st pregnancy
12.	38	27 S	++++	7 Penicillin	++++	40	-ve at 10/52	V.15 at 10/52 no trace	1) 4 years -ve 2) N.N.D. 4 days
13.	30-2	21 m	++++	2.4 Penicillin	++++	34	Cord Bl. + ve. N.N.D.	-	1st pregnancy
14.	34	36 m	++++	5 Penicillin	++++	37	Stillbirth (C.S.)	-	1st pregnancy
15.	30	26 m	++++	10 Penicillin	++++	40	-ve at birth	-ve at 8/12 (to date)	1st pregnancy
16.	30	23 m	++++	10 Penicillin	++++	38	-ve at birth	to date 3/12	?
17.	34	28 S	++++	7½ penicillin	++++	38	++ ve at birth (untreated)	Default	1st pregnancy
18.	36	36 m	++++	10 Penicillin	++++	40	no record	Default	1) Died at 15 yrs. 2) N.N.D. 1/12
19.	34	39 m	++++	10 Penicillin	++++	40	Cord Bl. +++ C.S.	Treated as C.S. 1 year -ve	Abortion at 4½/12
20.	38	24 m	++++	10 Penicillin	++++	40	-ve at birth +++ at 4-6/52	Treated C.S. 4/12 -ve	1st pregnancy
21.	28	34 m	++++	Nil	++++	34+	Stillbirth (C.S.)	-	6th pregnancy - not examined.

m = married
d = divorced
S = single

Results.

Consideration of the findings in this Group makes appalling reading. A summary is first given and then each section is considered in some detail.

a) Stillborn infants	3
b) Neo-natal deaths	1
c) Congenital syphilis	5
d) Alive and apparently well at birth (Early defaulters in 10 cases)	<u>12</u>
		21
		—

(a) Stillbirths.

Of the 3 stillborn infants, 2 were found to have congenital syphilitic changes at post-mortem.

(i) The mother was treated at 34th week of pregnancy with 5 mega-units penicillin. The foetal heart was heard after the completion of treatment. It has been mentioned at one time that massive dosage of penicillin might be lethal to the foetus but young infants tolerate large doses well and there is no obvious reason why the foetus should not do likewise. More likely the foetus succumbs to the overwhelming syphilitic infection.

In this case the mother was admitted in labour. No foetal heart was heard on admission and she had not felt foetal movements for some days. Delivery of a stillborn infant occurred.

Histo-pathological report - Congenital syphilis.
Placenta - syphilitic appearance.

(ii) The mother reported at 28 weeks and was diagnosed syphilis. She did not report for anti-syphilitic treatment or general ante-natal care despite repeated requests. She was brought into hospital in labour at thr 34th week. The foetus was macerated. Post mortem findings - congenital syphilis.

(iii) In the remaining case, the patient was treated with arsenic and bismuth, treatment starting at the 34th week. At 38-40 weeks she was delivered of a stillborn infant. No post mortem was carried out.

(b) Neo-natal Death.

In this case, the mother was treated with 2.4 mega-units of penicillin at 32 weeks. As the course finished, the patient went into premature labour. At birth the infant weighed 4 lbs.10 ozs. Cord blood and venous blood (heel puncture) was taken at birth and both were positive. Before the result was to hand, the infant died. Permission for post-mortem was refused. Prematurity and causes such as lung atelectasis may have been causal factors but nevertheless syphilis is a most likely suspect.

(c) Congenital Syphilis.

These 5 cases were diagnosed as serological results alone, the infants being clinically clear.

The school of thought which prefers to observe for 3/12 infants whose blood is positive at birth, arguing that often the infants' positivity is due to maternal antibodies crossing the placental barrier would criticise the diagnosis of congenital syphilis in two and probably three of the 5 cases. In these 2 cases the cord and venous bloods were strongly positive. The third infant was still strongly positive at 8 weeks but otherwise appeared to be healthy. Then three infants were treated as cases of congenital syphilis ... the medical officer preferring not to risk the babies in view of the lateness of treatment. It is true that the first 2 may well have been non-syphilitic although in the remaining case, one would have expected the titre to be falling after two months. In the 4th case, the serology was still strongly positive at the end of three months. Congenital syphilis was diagnosed and treated. The baby was clinically clear and X-ray of the lung bones showed no abnormality.

The 5th case is of some interest ... the mother was treated with 10 mega-units of penicillin at 38 weeks. Delivery occurred at term. The baby's blood was negative at birth but at 4-6 weeks was strongly positive. A repeat test was similarly positive. Clinical and X-ray examination was negative. The infant was treated for congenital syphilis.

(d) Alive and apparently well at birth.

This section numbered 12 but of these 10 defaulted.

(i) 5 were never seen after discharge from hospital.

3 had positive serology at birth.

2 were not tested.

(ii) 3 were not seen until $2\frac{1}{2}$, 4, 6 months after delivery.

Letters and almoners' visits eventually produced a tardy appearance at clinic.

All three were negative at this time but default then recurred.

- (iii) 2 were negative at 3 weeks and 6 weeks but defaulted thereafter.

There are two satisfactory follow-ups and both are relatively early in surveillance,

1 at 8 months negative to date.

1 at 3 months ditto.

Thus out of a total of 17 infants, there is:-

Default	12
Satisfactory follow-up (2 cases of C.S.)	2
Follow-up in early stages	3
(the above 2 at 8 and 3 months and 1 C.S. at 4/12)		

General Points.

1) Previous Pregnancies.

- 3 - alive and well - negative serology
- 5 - alive: not tested.
- 1 - abortion at 4½ months.
- 4 - died; 4 days, 1 month, 2 months and 15 years respectively. The cause of death not known definitely in any case.
- 1 - congenital syphilis (interstitial keratitis).

2) Social Status. 7 out of 21 (1/3) were single.

(3) No treatment. Diagnosis (immediately) after Delivery.

First Seen	Stage	Treatment	W.R.at Del.	Delivered at (Wks)	Fate	Previous Pregnancies
1. In labour	Latent	Nil	++++	28	S.B.	2 abortions 24:26 wks.
2. In labour	.-.	Nil	++++	40	S.B.	Nil
3. In labour	.-.	Nil	++++	38	C.S.	Nil
4. In labour	.-.	Nil	++++	32	S.B.	1 abortion, 26
5. In labour	.-.	Nil	++++	35	S.B.	9th Preg.1-6 N 7) N.N.D.3/52 8) Abortim 24/52
6. 34 wks.	.-.	Nil	++++	34	S.B.	1 abortion at 28/52

1. Results.

The results in this group show:-

5 intra-uterine deaths

1 case of congenital syphilis.

In 4 out of the 5 intra-uterine deaths, syphilitic changes were found in the foetus and/or placenta at post mortem. In the remaining case (No. 1) no examination was carried out.

There was no obvious ante or intra-natal complication.

In the remaining case, the infant developed clinical manifestations of congenital syphilis and the serology strongly positive. Treatment was carried out. Follow-up 2½ years - infant negative.

2. Previous Ante-natal Care and Treatment.

The disease was not suspected during the ante-natal period and, of course, no treatment given. Yet all but one had undergone ante-natal supervision before 28/52 on district and in not one case had the routine Wassermann and Kahn reactions been performed.

One would think, at the present day, that the taking of a specimen of blood for the Wassermann and Kahn reactions and Rh factor would have been a routine procedure at the first ante-natal visit, whether to general practitioner or town or county clinic. But having seen a large number of women referred to hospital from district care because of general obstetrical complications, I can say quite definitely that the Wassermann reaction is carried out infrequently.

Those engaged in lecturing undergraduates doubtlessly inform successive classes from year to year of the importance of a routine Wassermann and Kahn test when the pregnant woman is first seen. Yet in practice outside hospitals it is not done. Even in some hospitals - usually smaller ones with no well organised clinics - it is not routinely carried out. The importance of it should be stressed and repeated so that if they absorb only one point concerning the problem of syphilis complicating pregnancy, it should be this one.

As a rider it might be added that if they do find a woman to have a positive Wassermann reaction, then she should be referred to hospital for further investigation.

Nabarro's (7) case can be used to illustrate a positive routine Wassermann test was obtained early in pregnancy. Nothing further was done. The child was brought to him in due course with manifestations of congenital syphilis. This type of case should not occur and neither should the ones in the foregoing table - where the patients reported for ante-natal care.

3. All were admitted as emergencies.

4 because no foetal heart could be heard (3 in labour and 1 ante-natally, premature labour supervening 3 days after admission).

Case 1 was admitted on account of premature labour.

The case in which congenital syphilis developed in the infant was admitted on obstetrical grounds - Prolonged labour, spontaneous delivery.

4. Previous pregnancies - 12.

- 6 - alive: all of one mother. The last 2 were tested and negative.
- 5 - abortions - all late.
- 1 - Nec-natal death at 3 weeks ? cause.

Group 3

Congenital Syphilis

16 cases

Diagnosis

These cases were diagnosed by :-

- (1) History, particularly family. In three cases only was syphilis of the parents discovered:- (a) 1 mother - general paresis: (b) 1 father - tabes dorsalis: (c) 1 father - mother blood strongly positive but with no clinical manifestations. Every attempt should be made to procure the attendance, if possible of parents and other members of the family for examination, and serological tests. The publicity given to the importance of the Rh test makes it easier to obtain blood tests in whole families without rousing suspicions and causing family trouble.
- (2) Clinical Examinations. All cases showed one or more of the stigmata of congenital syphilis - interstitial keratitis, Hutchinson's teeth, sabre shins, rhagades etc. but sometimes these were minimal in degree.
- (3) Serological Tests. These were strongly positive in all cases in this group.

The main point in this group was to differentiate between this type and latent syphilis. This was accomplished by the above methods and the subject has already been referred to under Group 2 - latent syphilis. (Investigation and Diagnosis)

Treatment and its Effects

10 cases had received prolonged courses of treatment - 2 to 6 years and all had had one or two courses of penicillin. Prophylactic treatment was given in each case. These retreated cases of congenital syphilis are not included in the next section (Group 4) prior to pregnancy.

6 previously untreated cases were discovered at the ante-natal clinic. One received arsenic and bismuth therapy. The other 5 were treated with penicillin and 2 of these were given a 10 week course of bismuth in addition.

The maternal blood was still strongly positive at birth in each case.

All the infants had negative serology at birth or after 6 weeks. This was to be expected since third generation syphilis is extremely uncommon. The infants of the freshly treated

cases were followed - 3 monthly bloods for 1 year. Attendance was good - 5 completing surveillance - and all infants were negative - clinically and serologically.

In this series there was no case of congenital syphilis complicating pregnancy which had not had treatment before delivery. Murrell (3) advises that an infant whose serology is positive at birth (the mother being an untreated case of congenital syphilis) should have a prophylactic course of penicillin. (1 to 2 mega units)

Group 4

PROPHYLACTIC TREATMENT DURING PREGNANCY

34 cases

The patients in this group had undergone treatment for acquired syphilis at periods varying from 6 months to 6 years. They all attended early in pregnancy and reported their previous infection. 13 cases had been treated for early syphilis - and 21 for latent syphilis - some of the latter having been discovered at a previous pregnancy elsewhere. The 34 cases in this group were all new cases, attending our clinic for the first time. They do not include any of the cases treated in groups 1, 2 and 3, of this series who subsequently became pregnant. From these, there has been a minimum of 31 confinements, prophylactic treatment being given in most instances. All infants were healthy.

All 13 previous early infectious cases had negative serology throughout. In the latent cases, all having had full anti-syphilitic treatment prior to pregnancy, 3 were negative before pregnancy and 18 were positive. This positivity was unaltered in titre throughout pregnancy.

Most of these patients were treated prophylactically. Initially a 10 weekly course of arsenic and bismuth was given and later penicillin was introduced. Today, these patients are given a course of 5 mega units of penicillin over 10 days. Several cases where the expectant mother was considered "cured" (see page 33) prophylactic treatment was withheld.

In all cases the infants had negative blood at birth or at 6 weeks. They remained healthy in the follow-up period. The surveillance recommended is - if the mother has been treated for syphilis within 2 years of pregnancy, the child should have a blood test 6 monthly. Follow-up was satisfactory in this group. This is not surprising when one considers these patients originally attended regularly for treatment and follow-up. On becoming pregnant they continued to co-operate and after delivery attended regularly with their infants for surveillance.

The Necessity for Prophylactic Treatment

The pregnant syphilitic woman has always been regarded as a potential source of infection for the foetus. For this reason she has been treated regardless of the amount of previous therapy.

Recently the necessity for prophylactic treatment has been questioned and anti-syphilitic therapy has been omitted in selected cases who have had what was considered adequate treatment prior to pregnancy.

Goodwin (8) for example gives a summary of reported cases as follows:-

587 women.....819 pregnancies
2 out of 749 cases proved to be syphilis....
these being due to patients not attending in pregnancy.
70 (8.7%) cases unsuccessful.....abortions, stillbirths
and neo-natal deaths.

Goodwin states - on the basis of these results one can recommend without equivocation that it is not necessary to administer anti-syphilitic treatment during every pregnancy and that treatment may be withheld if:-

- a) Mother has previously received 4 gms or more of arsenic or its equivalent and bismuth or at least 2-4 million units of penicillin or its equivalent.
- b) the Mother shows no clinical evidence of active infection.
- c) the Mother is sero-negative or positive in low titres only.

One is left to wonder if the possible causes of the 70 unsuccessful pregnancies were sought and if causes other than syphilis were shown to be responsible.

Also adequate follow-up before withholding treatment is not mentioned, It would appear, since the author advises withholding treatment while the blood is still positive in low titre - I take it diminishing as well - that cases adequately treated by their standards becoming pregnant soon after treatment receive no further treatment if the 3 above requirements are met. I do not think this an advisable procedure - the mother has not been definitely proved clear until surveillance is complete. Relapse may occur and did in at least 2 of their cases, provided re-infection can be ruled out. The same must have happened in Heyman & McCain's cases (vide infra)

Ingraham (9) also report success in withholding further therapy where the mother has received adequate penicillin therapy prior to pregnancy.

Heyman & McCain (4) stress careful selection and constant observations throughout pregnancy. The amount of therapy must have been adequate and the course of the disease after therapy satisfactory. These authors had the experience of withholding further treatment in 5 cases and finding 5 syphilitic children.

The procedure is therefore not without risk and if cases of congenital syphilis occur in this group it must mean that neither treatment nor surveillance have been adequate.

With regard to syphilis, where the blood remains positive in unaltered titre after adequate treatment, Heyman & McCain think that re-treatment can probably be withheld with safety but with one proviso. It is that the positive serology represents sero-resistance of an infection adequately treated and not an active infection. This is still an extremely difficult point although many workers have tried to differentiate on the basis of the height of the serological titre... not very satisfactory.

As stated above, most cases in this series had prophylactic treatment. I think it is justifiable to withhold treatment under the following circumstances:-

- 1) Patient received full anti-syphilitic treatment
- 2) Reversal of serology
- 3) Clinically and serology clear after -
- 4) Full surveillance (2-3 years)

A syphilitic woman should be strongly advised against becoming pregnant until full anti syphilitic treatment and follow-up have been carried out. If she does become pregnant and she has not been finally discharged, I think she must have prophylactic treatment.

When the expectant mother has had latent syphilis and the blood is still strongly positive, as it often is despite what can be considered adequate therapy, I do not think it is worth trying to distinguish between sero-resistance and active infection. The difficulty has already been mentioned. It is much simpler and probably safer for the foetus to give the usual prophylactic course..

Care of the Syphilitic pregnant woman during labour and in the puerperium.

This often leaves much to be desired - and the reason the subject is included at this point is because in the series there was one maternal death, occurring in a prophylactically treated woman.

The details of this case are worth recording:-

The patient was para 3. She had been fully treated for latent syphilis during her first pregnancy. Prophylactic treatment was given during the second and this, the third pregnancy. The first two infants had been followed up and both were healthy and the serology negative. The prophylactic course in the third pregnancy consisted of 4.8 mega units of penicillin. The ante-natal period was uneventful.

She was admitted at term in labour.....during the night. "Syphilis complicating pregnancy" was stamped across the top of her ante-natal record. Because of this the labour ward sister thought and the medical officer-on-duty agreed that she should not be admitted to the ordinary labour wards. There was an extra labour ward for "dirty" cases but this was in use. This patient was therefore sent to the block where the septic cases (puerperal sepsis, septic abortions etc) were treated. This block was separate and some distance from the maternity department. The patient was delivered by a member of the general nursing staff (night sister) who although a certified midwife had not been engaged in active obstetrics for years. The confinement took place in a cubicle where there was no adequate provision for obstetrical emergencies.

The 1st and 2nd stages of labour were normal, spontaneous delivery of a live and healthy looking infant occurring. In the 3rd stage, the patient suddenly collapsed. It was found that complete inversion of the uterus had occurred. The patient died.

It is well known that inversion of the uterus can occur spontaneously (about 13to4% of cases according to Munro - Kerr (10) But many occur as a result of mismanagement of the 3rd stage of labour. On questioning the staff concerned, no obvious mismanagement of the 3rd stage was apparent. However, in this tragedy, one cannot escape the facts that the patient was delivered in unsuitable surroundings by staff not actively engaged in obstetric practice. The outcome might have been different had she been delivered in the maternity block - as she should have been.

There is a marked tendency among the nursing staff and the medical staff in maternity departments as soon as they hear or see the words "Syphilis complicating pregnancy" to isolate the unfortunate woman - like a leper - into a cubicle. She is delivered there (or perhaps in a labour ward for "dirty" cases) and kept there with her baby until discharged from hospital. After she has been discharged, the cubicle is sealed off, furniture washed down or carbolised and through fumigation carried out. The room is then ready for further use. How often I have seen this process of events in hospitals with which I have been connected! I have questioned colleagues practising in various parts regarding the intra-natal handling of this type of case and it is obvious that the process of events described above is common and widespread. The fact that the vast majority of these women have been fully treated during pregnancy or received only prophylactic treatment is not considered.

If any type is a danger, particularly to the attendant it is the case of untreated syphilis (especially with early open lesions) complicating pregnancy which is admitted, usually as an emergency.

Yet this is the very type one does see from time to time. The infection is not recognised. She is delivered in the ordinary labour ward and transferred afterwards to the ordinary lying-in ward. The infant, if alive, goes with her or to the ordinary nursery. Some days later she is found to be syphilitic, usually when the routine bloods taken on admission return. Then the process of isolation etc. begins.

In most maternity units, the person engaged in delivering mothers takes full antiseptic precautions and wears masks, gown and gloves to prevent infection of the mother. These precautions also serve to protect efficiently the accoucheur in the syphilitic case especially if undiagnosed and/or untreated. When the placenta is being examined gloves should also be worn. After delivery, if the sorbo-rubber pad of the labour bed is washed down and the sheets changed - as happens after every delivery, then there can be no chance of infection following mother in labour. Presumably it is fear of this that keeps the syphilitic mother from being allowed into the ordinary labour ward. If one wished to add an extra precaution then one could leave the particular labour ward unused for the next hour and as *Sp. pallida* cannot live in air for more than this time, complete safety exists. This should satisfy nursing personnel but it doesn't.

Again in the maternity units of today there is or should be meticulous attention to prevention of infection generally of the lying-in mother - full antiseptics during various procedures such as catheterising, care with swabbing, etc. With this general care the syphilitic mother is no danger. The one type of case which may be of danger is the early case with open lesion. I think this type of case should be isolated. She is easier to treat and nurse generally as care must be taken to see that she has her own feeding utensils, and toilet articles. It is to be noted that if there is breach of the above intra- and post-natal precautions, then there is danger. I know of one midwife who developed a primary sore on the finger after delivering a syphilitic mother with open early lesions (no gloves worn during delivery)

It may be said that the syphilitic mother is not a danger provided the above precautions are taken and I think she should have the same care during labour and in the puerperium as the ordinary patient.

DISCUSSION.

(1) Consideration of results in the present series

The clinical groups have been discussed individually and the results obtained in the series must now be considered. The most important aspect of the subject is obviously that of acquired syphilis previously untreated, in the expectant mother.

In congenital syphilis complicating pregnancy there is only a very slight risk of transmission of infection to the infant. If the patient receives a full course of treatment during pregnancy that risk is practically eradicated. Murrell has had one case of 3rd generation syphilis occurring after adequate treatment of the mother. In acquired syphilis if a woman has had adequate antisyphilitic therapy but has not completed surveillance before pregnancy, a prophylactic course of treatment is given in the ante-natal period. With this it may be taken that the infant will be free from syphilis. It is now generally considered that a prophylactic course is unnecessary if the mother is "cured". These statements regarding prognosis were confirmed in this series, no cases of congenital syphilis occurring either in groups 3 or 4 in a combined total of 50 pregnancies. These results are highly satisfactory and further review is not necessary.

The analysis of results will therefore be confined to previously untreated acquired - early and latent - syphilis complicating pregnancy (i.e. groups 1 and 2 of this series.

A total of 102 cases is available for survey.

The results are discussed under 4 main headings:-

- a) Results of early and latent syphilis complicating pregnancy - including treated and untreated cases.
- b) Results in acquired syphilis treated (including arsenic and bismuth therapy) during pregnancy.
- c) Results of penicillin treatment (alone or combined with metal therapy) in acquired syphilis complicating pregnancy.
- d) Results where no treatment is given prior to delivery.

- a) Results of early and latent syphilis complicating pregnancy - treated and untreated.

The objects in this section are to demonstrate the results obtained and to assess the effect of the complicating syphilitic infection on the outcome of pregnancy.

The results are shown in the following tables:

Stage.	Diagnosis.	Treated in . Preg. cy	Number.	Alive.	Con. Sy (Alive)	Unsucc- essful outcomes.	Default Rate.
Early Syphilis (37 cases)	Before 28 wks	Yes	20	19	0	1 late abort:	1 out of 19
	After 28 wks	Yes	11	5	1	3 SBs: 3 NNDs.	1 - 5
	After delivery	No	6	4	1	2 NNDs	3 - 4
Latent Syphilis (65 cases)	Before 28 wks	Yes	38	36	2	1 late Ab: 1 S.B.	13 - 16
	After 28 wks	Yes	21	17	5	3 SBs: 1 NND	12 - 17
	After delivery	No	6	1	1	5 SBs	0 - 1
	Total:		102	82	10	20	30 - 82

1) From the study of the 102 cases of early or latent syphilis seen for the first time during pregnancy or labour there were:-

- a) 82 live infants on discharge from hospital
- b) 20 unsuccessful outcomes.

2) In the 20 unsuccessful pregnancies there were:-

2 late abortions - no histo-pathological examination was made.

^{...}
11 12 stillborn infants - in 9 of these cases at postmortem examination, syphilitic changes were found in the foetus and/or placenta. In the remaining 3, no post mortem was carried out.

^{...}
111 6 neonatal deaths - 3 infants dying at 1, 16 and 24 days were definitely proved to have congenital syphilis at post-mortem examination. In the remaining 3 syphilis was not demonstrated. One died of broncho-pneumonia - only a section of lung (showing overwhelming broncho-pneumonia) was examined and no general search - liver etc., was made for evidence of syphilitic infection. No post-mortem was carried out in the other 2 infants - one dying on the 3rd day had positive serology at birth.

Thus in 12 cases there was definitely proved syphilis and it is reasonable to attribute these intra-uterine and neonatal deaths to the infection. In the remaining 8 or in some of these it may well have been the causal factor. However, as autopsies were not performed - or, as in 1 case, performed incompletely the deaths cannot definitely be attributed to syphilitic infection.

The obstetrical records of all these cases were reviewed. In no instance was there any obvious obstetrical cause such as pre-eclamptic toxæmia, ante-partum hæmorrhage, foetal abnormalities, erythroblastosis foetalis, maternal conditions such as diabetes mellitus, etc. to account for intra-uterine death. With regard to the neonatal deaths, there were no complicated labours. In 4 cases where the infant died in the first month of life, labour was premature occurring at 34, 34, 34 to 36, 36 weeks respectively. The smallest infant weighed 4 lbs 6 ozs and the largest 5 lbs 1 oz. so all, if prematurity was the only factor involved, had a very good chance of survival especially as there is a first class premature baby unit attached to the maternity department. In the 3 neonatal deaths where syphilis was demonstrated, the infants were premature. The deaths may have been due to syphilis + prematurity but I would put down the former as the primary cause. Might it not be that the prematurity and neonatal death were both due to syphilis?

3) 10 cases of congenital syphilis were diagnosed in a total of 82 infants. It may be that 2 of these infants were not syphilitic - namely, the two treated at birth because of positive serology at that time. Some may object to a third case - namely the case where the blood tests were still strongly positive at 2 months. However, the remaining 7 were definite cases of congenital syphilis and I think probably the last mentioned case also, for one would be expecting the titre to be falling by the end of the second month.

- 4) Default rate. There were 30 instances of default where the mother was discharged from hospital with a live infant. It is proposed to deal with this subject separately later in the discussion.
- 5) In the series, at least 30% of the pregnancies (and most probably more in view of the numbers of defaulters) culminated in stillbirths, deaths in early infancy or live congenital syphilitic infants.

These results are not good and show that syphilis even today in the penicillin era is still responsible for an appreciable number of deaths in utero and in early infancy. These results are capable of improvement and the factors concerned in this are discussed in the final section. If this were achieved it would mean in any given unit - a further improvement in the already falling stillbirth and neonatal death rate - a subject in which obstetricians and paediatricians are vitally interested.

6) Results in acquired syphilis treated during pregnancy
(including arsenic and bismuth therapy)

The table below gives the overall results in cases treated between 1942 and August 1952. It is proposed not to discuss these results in detail as they include cases treated by arsenic and bismuth therapy alone, this form of treatment being, to all intents and purposes of historical interest only. Penicillin (either alone or combined with metal therapy) being now the chief agent in anti-syphilitic treatment, the results following this form of therapy will be discussed in the next section.

Briefly, the results in the 15 cases treated by arsenic and bismuth are as follows:-

- i 9 infants alive and apparently well but 4 defaulted within 4 months: surveillance in the remainder was satisfactory.
- ii 1 late abortion and 3 stillborn infants, one being shown at post-mortem examinations to have congenital syphilis.
- iii 1 infant was syphilitic - untreated
- iv 1 died at 6 weeks - broncho pneumonia

Stage.	Diagnosis.	Number.	Alive.	Con. Sy. (Alive)	Unsuccessful outcomes.
Early Sy. 31 cases	Before 28wks	20	19	0	1 late abortio 3 SBs) 3 deaths)
	After 28wks	11	5	1	
Latent Sy. (58 cases)	Before 28wks	38	36	2	1 late abortio 1 SB) 2 SBs) 2 deaths)
	After 28wks	20	17	5	
TOTAL		89	77	8	12.

c) Results of penicillin treatment in acquired syphilis complicating pregnancy.

74 cases were treated with penicillin alone or combined with bismuth or arsenic-bismuth therapy. For the last 4 years penicillin alone has been used. How this method of treatment came to be accepted has previously been outlined.

The results obtained are given in the following table:-

Stage.	Diagnosis.	Number.	Alive.	Con. Sy. (Alive)	Unsuccess- ful Outcomes	Default Rate
Early Sy. (23 cases)	Before 28wks	15	15	0	0	1 out of 15
	After 28 wks	8	4	0	2 SBs (1 C.S.) 2 deaths ")	0 - 4
Latent Sy. (51 cases)	Before 28wks	34	33	2	1 late Ab.	12 - 33
	After 28wks	17	15	5	1 S.B. (C.S.) 1 death (no PM)	10 - 15
TOTAL		74	67	7	7	23 - 67

There were:-

- a) 7 cases of late abortion (1), stillbirths (3) and death in early infancy (3 - at 3 days, 3 and 5 weeks respectively) In 3 of these - 2 stillbirths and 1 neonatal death, evidence of congenital syphilis was found at autopsy. In the remaining 4, no post-mortem examination was performed.
- b) 7 infants treated for congenital syphilis. 4 of these were definitely proved cases of congenital syphilis and one infant was probably infected, the Wassermann and Kahn reactions being strongly positive at 8 weeks. The remaining 2 were treated on account of strongly positive serology at birth.

Thus 7 out of 74 (9.5%) were definitely known to be syphilitic and if the probably infected infant be included, there is a 10.5% incidence of congenital syphilis in this series.

The above figures are not nearly so good as those of some American authorities and yet the figures given presents the picture at its most favourable. It may be worse because:-

- i The 4 cases of late abortion, stillbirth and death in early infancy not examined may have been syphilitic. Also, the 2 cases with strongly positive serology at birth and treated because of this may have definitely been luetic.
- ii Out of a total of 60 infants discharged to surveillance and untreated there were 21 instances of default (35%) When one considers, for example, the defaulters occurring in women treated for latent syphilis after the 28th week of pregnancy (see pp²⁶ and below) then it would not be in the least surprising if some of these infants were syphilitic.

As regards this series I would say that penicillin therapy in the treatment of acquired syphilis complicating pregnancy is -

- a) Highly satisfactory in early syphilis (primary or secondary) where the treatment is commenced before the 28th week. All 15 pregnancies resulted in live, healthy infants, each being negative at birth and thereafter. Follow up was satisfactory.
- b) In the cases of latent acquired syphilis treated before the 28th week. The results, on the whole, were again satisfactory, but 2 cases of definite congenital syphilis did occur in this group.

It has been stated by many authorities, that provided anti-syphilitic treatment is commenced early in pregnancy a healthy infant will result. These 2 cases prove that this is not always so. This finding has also been noted by Ingraham.⁹ In his series there were 6 cases of congenital syphilis resulting in mothers treated for acquired syphilis (he seems to combine primary, secondary, and early latent syphilis) before the 20th week of pregnancy. This recurrence was attributed to relapse towards the end of pregnancy.

As a result of these unexpected cases, this group presents a problem which I had not suspected previously. Possible methods of overcoming it have been discussed on pp.19

c) In both early and latent syphilis treated after the 28th week of pregnancy, the figures are far from satisfactory. I cannot agree with Earle Moore's statement that results are equally good when the expectant mothers are treated late.

From 8 mothers treated for early syphilis, only 4 infants survived. There were 2 stillborn infants and 2 deaths at 3 and 5 weeks. In one of each syphilis was shown to be present but in the other 2 no examination was made.

In 17 women treated for latent syphilis there were:-

- i 5 infants treated for congenital syphilis (probably three definite cases)
- ii 1 stillborn infant (congenital syphilis) and 1 neonatal death (cord blood + ve and died on the 3rd day - no post-mortem.
- iii Of the 10 remaining cases, 8 defaulted, 5 of them were never seen after discharge from hospital, 3 having positive serology at birth.

With one exception, all cases received 2-4 mega units or more of penicillin. One case of secondary syphilis treated after the 28th week received only 0.6 mega units and was delivered of a macerated foetus soon afterwards.

Penicillin is generally agreed to be the most powerful antisyphilitic agent. But it has been shown that cases of congenital syphilis can and do occur after penicillin therapy. Even with penicillin, the need for early diagnosis and prompt treatment is as great today as ever. It's use does not obviate the need for careful follow up.

d) No treatment given prior to delivery.

Stage	Number	Alive	Con. Sy (Alive)	Unsuccess ful Outcomes.	Default Rate
Early	6	4	1	NNDs 2 ↓ CS	3 - 4
Latent	6	1	1	5 SBs(4CS)	0 - 1

Of the 4 infants who were discharged alive from the early syphilitic mothers - (one) developed congenital syphilis, 2 were not seen after discharge from hospital and 1 was negative at 6 weeks but default occurred thereafter. It may well be that not a single healthy infant has been obtained in this group. Handling of infants born alive of untreated mothers is discussed under "Basis for treatment"

(2) Consideration of results in other series

Some American authorities such as Ingraham, Goodwin, Earle Moore and Tucker have presented series in which the results were much more favourable than those obtained in the present series.

Ingraham (9) - found in 663 cases of acquired syphilis treated during pregnancy, 10 cases of living congenital syphilis (1.5%) 77% of these cases were followed up for 6 months and many (no actual figures) up to the age of 1, 2 or more years. There were 28 stillbirths and 10 neonatal deaths. There are no details regarding these and no investigation seems to have been made. He may not have been unduly concerned about these as there was a 92.5% rate of healthy children born of syphilitic mothers as compared with 86% in a large control (non-syphilitic) series. The latter figure would certainly cause consternation if it occurred in our maternity departments.

Goodwin (8) - reviewing 850 cases reported in the literature up to 1.1.50 found 15 cases of congenital syphilis - less than 2%

Earl Moore (11) - reviewing the combined figures of the University of Pennsylvania and John Hopkins Hospital found 1 case of congenital syphilis (0.8%) and 3 late abortions in 121 pregnancies. 19 out of 84 were followed up for less than 2 months and a total of 43 out of 84 for less than 6 months. In 28 cases, the total penicillin dosage was 1.2 million units or less. This is much below the dosage now recommended yet the results were extremely favourable.

Tucker (12) - in this series there was no case of congenital syphilis in 149 syphilitic women treated during pregnancy.

Not all results are quite so favourable. The combined series of Cole, Schaffer and Thomas (13) shows a higher incidence of congenital syphilis. I think their figures are of considerable interest and they are reproduced in the following table.

Infants born of Pen Treated Mother with Early Syph:	Syphilis in infant dead or alive		Other accidents of pregnancy - almost certainly not due Syphilis (misc. S.B.)	Infants born alive. Normal.
	Definite.	Questionable.		
176	4 2.4%	3 1.7%	10 (5.6%)	159 x 90.3%

x includes 9 infants dying at various ages - no definite evidence of syphilis in any and syphilitic infection definitely excluded in 4.

a) In this series there were 10 cases of abortion and stillbirth almost certainly not attributable to syphilis. Syphilis is a very definite cause of abortion (late) and stillbirth. It would be interesting to know how the above conclusions were reached.

b) There is a considerable proportion of unfavourable outcomes to pregnancy - 10 abortions and stillbirths: 9 infants died: 7 cases of proved or questionable syphilitic infection some of whom evidently did not survive... a total of 26 which seems a considerable number to me. There were therefore 150 who lived and were apparently free from infection.

One wonders after perusal of the above table if the incidence of congenital syphilis might not be higher than that shown (2.3% + 1.7%)

The figure of 1 to 2% of congenital syphilis following penicillin therapy in the syphilitic expectant mother is widely published and accepted. This figure seems (in some series at least - such as Ingraham's) to apply to cases in which the child is alive and infected.

In my opinion, all cases of late abortion and stillbirth should be subjected to careful examination for evidence of syphilis. The fact that the incidence of these may be no higher or even lower than in a control group (as Ingraham seemed to find) does not exclude the necessity for examining each late abortion and stillbirth. Similarly all infants dying in the neonatal period or after should be examined post-mortem for evidence of syphilis. If such evidence is found, these cases should be added to the living cases of congenital syphilis, thus giving an overall picture of the effect of syphilis when treatment has been given during pregnancy. In some series it would appear that such examinations are not always carried out e.g. in the series of Cole, Schaffer and Thomas. In a series of 341 cases reported by Cole (14) there were 325 infants alive. In the 16 unsuccessful outcomes, only one post-mortem was performed.

With regard to follow up, what appears to be rather short periods of time are suggested. Earle Moore (11) states that the child must be followed up for 3 months at least. In the combined series - Cole, Thomas and Schaffer 80% were followed up for 3 months or more. Ingraham's (9) series showed a 77% follow up for 6 months and he states many were followed up for 1, 2 years or longer.

Goodwin (8) goes as far as to state that a completely negative examination at the age of 4 months is a guarantee that the infant has escaped congenital syphilis. However, I think a short surveillance period is dangerous because:-

- a) Syphilis may appear for the first time after 4 months. In 77 cases of congenital syphilis occurring in a 4 year period reviewed by Hayman and McCain (4) syphilis was found in 2 of the cases at the 5th and 7th month, follow-up having been carried out since birth.
- b) Murrell (3) has seen cases develop signs and positive tests of syphilis later despite negative serology up to 6 months or even longer.
- c) It is accepted that a foetus in utero already infected may be cured by penicillin administered to the mother. In adults, the therapy given may not be sufficient to cure an early infection but may cause reversal of serology for a time, relapse occurring later. Might not a similar process of events occur in the foetus so that in the early months of infancy, the child may be serologically and clinically clear. Relapse in such a case may occur months after.

Finally, penicillin therapy has now been in use for a considerable period. There has been a diminution (as compared with the days of arsenic and bismuth therapy) in the incidence of congenital syphilis in the centres from which these series were published. On account of the excellent figures given, one would have expected their methods to be widely followed in other clinics in the U.S.A. resulting in further decrease. However, the statistics quoted in the Journals of Venereal Disease Information and Paediatrics (15) show that the number of reported cases of congenital syphilis has remained constant between the years 1946 and 1951. There are approximately 14,000 per annum and 20% of these are infants under 1 year. The Public Health Service estimates that there are 100,000 children of 10 years and under of undiscovered congenital syphilis. These are sobering figures and indicate that even in the U.S.A. there is still a real problem to be tackled and overcome in spite of the very favourable results in these individual large centres.

(3) Default

Not infrequently in V.D. clinics, patients of social irresponsibility and ignorance are encountered and a tendency to default is common.

In the present series 30 out of 82 mothers who were discharged with living infants defaulted. This is a high figure and should be considered when reviewing the problems of syphilis complicating pregnancy.

When the disease was diagnosed early in pregnancy there was satisfactory attendance for treatment, follow-up and general ante-natal care. Once the condition was diagnosed, its nature with possible effect on the baby was explained. The necessity for regular post natal attendance for both mother and infant - who might need treatment at birth or subsequently depending on the result of investigation - was emphasised. Despite advice, 14 out of 55 of mothers treated for early or latent syphilis before the 28th week of pregnancy defaulted.

Of 22 cases of early or latent syphilis treated after the 28th week 13 defaulted - 2 of these infants actually having been treated at birth as cases of congenital syphilis on account of positive serology. A high default rate is not surprising in women who ignore until the latter weeks of pregnancy the widely known value and availability of ante-natal care.

3 out of 5 cases who were admitted in labour and the disease discovered at that time defaulted. The mothers were treated but it was decided to observe the infants. Two were never seen after discharge from hospital and one was negative at 6 weeks, default occurring after this.

In all instances where default occurred every effort, by frequent letters and almoner's visits, was made to obtain the attendance of the mother with infant at the clinic.

Of the 30 cases, 14 were never seen after discharge from hospital, 8 of these having been treated late in pregnancy or received no treatment prior to delivery. 6 defaulted for periods varying from 2½ months to 6 months after discharge from hospital. These patients as a result of frequent letters and the efforts of the almoners were seen with their infants at these times. After this one visit default recurred. One of these infants seen at the 3rd month had a very strongly positive Wassermann and Kahn reaction and may be taken to be suffering from congenital syphilis. The mother refused to bring the child to the clinic for further investigation and treatment. In the remainder (10) default occurred between 3 weeks and 6 months, the blood tests being negative at these times.

Stage	Time of Diagnosis	Default Rate	Time of Default
E A R L Y	Before 28wks	1 out of 19	1 on discharge from hospital
	After 28wks	1 - 5	1 at 3 months (WR +++)
	After delivery.	3 - 4	(2 defaulted on discharge from hos: (one at 6 weeks.
L A T E N T	Before 28wks	13 - 36	(6 on discharge from hos: (7 between 2 and 4 months
	After 28wks	12 - 17	(5 on discharge from hos: (7 between 3/52 and 6 months
	After delivery	0 - 1	-

I believe this question of default to be a very important consideration in the problem of syphilis complicating pregnancy. I have the impression that sufficient attention is not paid to it and hence it has been dealt with in some detail.

In the articles which I have perused including those mentioned in the previous section, no attention was given to this question except in one of Goodwin's articles. In it she mentions that if there is any doubt about follow up treatment is better given in the lying-in period. However, from this series it can be said that default is extremely common and I believe that it should be a main factor of consideration when assessing the advisability of treating an infant.

(4) Diagnosis of Congenital Syphilis

It is proposed to discuss this question under 2 headings :-

- a) diagnosis in the stillborn infant
- b) diagnosis in the living infant.

a) Principles of diagnosis in the still-born infant.

Every stillborn child should be subjected to an autopsy. In every stillborn infant delivered of a syphilitic mother it is most important to look for evidence of syphilis.

The main diagnostic features are :-

- i Maceration - if the foetus is macerated, this in itself is suspicious. F.J.Browne (5) states that about one third of all macerated foetuses are syphilitic.
- ii Liver - is invariably infected and may be enlarged. Periportal cirrhosis or inter-cellular cirrhosis may be found. Occasionally miliary gummata are present.
- iii Spleen - may be enlarged.
- iv Lungs - may show changes in the forms of an increase of interstitial tissues in the alveolar walls so that the walls are thickened and the alveolar spaces diminished. The endothelial cells lining the alveoli are shed into the lumen which they loosely fill - pneumonia alba..
- v Chondroepiphysitis - the jagged irregular chondro-epiphyseal junctions may be present.
- vi Sp. pallida may be demonstrated in soft organs such as the liver and spleen and supra-renal glands.
- vii Examination of placenta - should also be carried out. The classical appearance of the syphilitic placenta is wellknown. Again Sp. pallida may be demonstrable.

Careful pathological examination on these lines should be carried out on every stillborn infant delivered of a syphilitic mother, treated or untreated. If evidence of syphilis is found then it is

reasonable to attribute the cause of stillbirth to this (provided that no acute obstetrical emergency such as placenta praevia led to sudden death of the foetus in utero) Such cases should be included when assessing the incidence of congenital syphilis in a review of syphilis complicating pregnancy.

b) Principles of diagnosis in the live infant

i Demonstration of Sp. pallida from the wall of the umbilical veins. This procedure may be adopted in cases where there is reason to believe that the child may be infected e.g. in mothers with early acquired syphilis where the serological test is positive at delivery. The specimen taken from the intima of the umbilical vein is examined under the dark ground illumination microscope within an hour of birth. Less preferably, silver staining methods (Levaviti, Fontana.) may be used. The piece of cord for examination should be taken as close to the foetal end as possible. Should Sp. pallida be present, the diagnosis is absolute and the problem of positive serology at birth is obviated. This procedure although described in most textbooks does not seem to be widely followed. I think it is worth carrying out and diagnosis has been made by this method in one of our cases recently. It may, however, be very difficult to demonstrate the organism and failure to do so does not exclude syphilis.

ii Significance of positive Serology at birth

There are two schools of thought on this subject:-

- (1) Transfer of Wassermann reacting bodies from the maternal circulation may give rise to a false positive reaction in the infant. The serological reaction diminishes in the titre and usually becomes negative in the course of 4 to 6 weeks. In Ingrahams (9) series 46.1% of infants who turned out to be non-syphilitic had a positive blood test at birth. In almost every case the blood test became negative within a month and only occasionally did the syphilitic reagin remain in perceptible amount for as long as 2 to 3 months. This is the view and basis of practice of many authorities.
- (2) Others such as Murrell (3) and Wile (16) believe that positive serology at birth is presumptive evidence of foetal infection and act on this.

Murrell never presumes on cord blood alone - only on venous blood obtained often from an arm vein. MacLachlan (17) recommended the use of venous blood obtained by the heel stab method in view of the high percentage of anti-complimentary results obtained with cord blood.

There is no doubt that many non syphilitic infants have positive serology at birth and this reverts to negative within the first few weeks of life. A number of our cases behaved in this way. On the other hand, the positive serology may be due to syphilis in the infant. In conjunction with the results obtained in this series and the likelihood of default, I would say it is justifiable to regard positive serology at birth as presumptive evidence of syphilis and treat accordingly, particularly where the mother has been treated for acquired syphilis late in pregnancy. This subject is referred to again in the next section.

In many clinics an appointment is given to the mother for attendance with infant (untreated and regardless of serology) 6 weeks after birth for clinical and serological assessment. This procedure was carried out in some cases in this series and 3 of our infants died within this period, one definitely from congenital syphilis, Under the regime favoured by Murrell & Wile, such infants would be protected against the possibility of a missed diagnosis in the first few weeks of life and against the lack of co-operation and ignorance of the parents at that time and later.

If a mother had received full antisyphilitic treatment before pregnancy and a prophylactic course during the ante-natal period; and if the child had positive serology at birth, then I would regard this as transfer of maternal reacting bodies into the foetal circulation and would observe only.

Where a child is untreated and under surveillance there should be at regular intervals

- a) complete clinical examination - general condition, inspection of skin surfaces, muco-cutaneous junctions and mucous membranes: lymphatic glands, also hepatic and splenic enlargement should be sought.
- b) Serological tests.
- c) Xray examination of long bones for demonstration of periostitis or the epiphyseal changes of osteochondritis.



(5) Basis for treatment of congenital syphilis

Taking into consideration

- a) results in the present series
- b) high default rate
- c) difficulty in interpretation of serology at birth

it is possible to suggest a basis for investigation and treatment of infants born of syphilitic mothers.

This basis can be suitably discussed in 3 groups, depending on whether the patients were :-

- (1) treated before the 28th week of pregnancy
- (2) treated after the 28th week
- (3) not treated before delivery

(1) Treated before the 28th week

Early syphilis. In cases of primary or secondary syphilis treated early in pregnancy it has been our experience that in almost all cases the maternal serology has reverted to negative before delivery. Negative serology and freedom from infections are to be expected in these infants. They should have regular surveillance - 3 monthly up to 2 years.

Should strongly positive serology persist up to the time of delivery, then it is very likely that the maternal infection is not controlled and there is a possibility that the infant may be infected. Treatment is advised.

Latent syphilis. In the series it was found that the majority of mothers were still strongly positive at time of delivery. The maternal infection may or may not have been controlled. If the child's serology at birth is negative there should be surveillance as above.

Where the infants blood tests are positive treatment should be given:- 2 of the babies in this group, as has been detailed previously were syphilitic.

(2) Treated after the 28th week

Early syphilis. If the maternal serology is negative at time of delivery or positive in greatly diminished

titre and if the infants serology is negative, then surveillance can be carried out - monthly for the first 3 months (in case negative findings are temporary only ^{due} to maternal penicillin and the child is in fact infected) and 3 monthly thereafter up to 2 years. Our results were not good - but in the 4 cases where the mother's blood was negative before delivery, the infants were free from infection. However if the Wassermann and Kahn reactions are still positive at birth then there is risk of infection to these infants. They should be treated for congenital syphilis. In the 4 cases in this group where the maternal serology was positive at birth, there were 2 stillborn infants and 2 deaths in early infancy within 6 weeks.

Latent syphilis. In this group, the mothers were all strongly positive at delivery. There was a high incidence of congenital syphilis and of default. In my opinion these children should have antisyphilitic treatment.

(3) Not treated before delivery

In cases of either early or latent syphilis where one is fortunate enough to obtain a living child, immediate antisyphilitic treatment should be given to both mother and infant. I would say there is absolutely no place for leaving untreated and discharging to surveillance.

Earle Moore (18) believes that treatment should be withheld until the presence of syphilis is definitely established his reasons being:-

1. Risk of treatment is present just as in the adult. With the introduction of penicillin which is very well tolerated by these infants and constitutes the modern method of treatment, this objection is not nearly so great as previously.

2. Serious social and economic problems arise. The mother will, however, have to attend for further treatment and/or surveillance, and the infant for regular assessment. I find it difficult to understand how a course of treatment per se can give rise to these problems.

3. Such delay as may occur provided all available methods of study are employed does not materially prejudice the child's prognosis. Black (19) supports this view - a delay of 6 to 8 weeks in instituting treatment in an apparently healthy infant does not jeopardise the chances of ultimate cure. I am not convinced - as 3 of our infants who appeared healthy on discharge - died before the 6th week, one showing congenital syphilis at post-mortem examination.

In criticism of our policy it might be said that one could not assess accurately the number of absolutely proved cases of congenital syphilis occurring in the unit. Also infants who were not in fact syphilitic were being treated.

In any event, in this series one cannot say what the exact incidence of congenital syphilis was. In the default group - there was one known case of untreated congenital syphilis - and there are other potentially infected cases. Some are very likely indeed to be infected, eg. the infants whose mothers who received no treatment before delivery or late in pregnancy.

I would prefer to treat some non syphilitic infants rather than allow some who were actually infected to go untreated through default. Thus their subsequent appearance perhaps many years later suffering from serious and perhaps irremediable effects of the disease would be prevented.

The basis for treatment given closely agrees with the rules adopted by Murrell (3) which may be summarised as follows:-

1. All babies are treated as acute cases of congenital syphilis if the mother suffering from acquired syphilis has had no previous treatment.
2. All babies of mothers with early acquired syphilis who still have positive blood tests at the time of confinement are treated for congenital syphilis.
3. Latent cases where the babies blood is positive at birth - are also treated.
4. Babies of mothers who have had adequate treatment in pregnancy and negative serology at time of confinement have 3 monthly clinical examinations and blood tests up to 2 years.
5. Murrell also recommends:-
 - a) If the mother has been treated within 2 years of pregnancy, the child should have a blood test 6 monthly for 2 years.
 - b) Should a congenitally syphilitic mother be delivered of an infant with positive serology at birth, that infant should be treated with one prophylactic course of penicillin.

The therapy given to these infants may be briefly mentioned.

Where the baby is suffering from congenital syphilis penicillin is given by intra muscular injection in a course of 2 to 4 mega units in divided dosage over 10 to 14 days. This course can be repeated on one, two or three occasions depending on response to therapy.

Where a prophylactic course is considered necessary e.g. para 5 (b) above, a single course of penicillin, 1 to 2 mega units is given.

(6) Factors involved in decrease of congenital syphilis

That there is still room for further reduction in the incidence of congenital syphilis there is little doubt. Therefore, in this final section it is appropriate to discuss methods whereby the occurrence of the disease may be decreased. Most of these points have already been mentioned throughout the thesis. The following is a resume of the combined factors affecting the incidence of congenital syphilis.

Early ante natal care

If good results are to be obtained then this is a necessity. A glance at the first table in the section "Consideration of results in present series (p. 37) will show that the incidence of congenital syphilis, stillborn infants and death in early infancy is much higher in cases treated after the 28th week of pregnancy or not treated prior to labour. 44 out of 102 patients were treated after the 28th week (31) or received no treatment before delivery (13)

There is often an unfavourable personal or social background in these patients. Also the present day availability of ante-natal care and its great value is well known to the public. Therefore, although early ante natal care is an essential for really satisfactory results in syphilis complicating pregnancy it is difficult to suggest practical steps whereby this might be ensured.

Routine blood tests

(a) In hospital practice, blood should be taken for Wassermann and Kahn reactions at the first visit.... rather surprisingly, it is not always done. If positive then there is need for further immediate investigations - and if the diagnosis be confirmed immediate treatment.

Also some authorities favour a routine blood test at the 36th week of pregnancy. Heyman and McCain (4) in a review of 77 cases of congenital syphilis found that in 21, the mother's blood tests had been negative at first attendance. This type of case was not a feature of this series although it did occur in 2 instances. Therefore, a test at this time may be of help in averting the occurrence of a few cases of congenital syphilis.

(b) General practitioners should always take blood for Wassermann and Kahn reactions at the first visit of the patient.

This routine blood test is very frequently omitted on district. Should the mother be syphilitic the result for the foetus or infant is often disastrous. When a blood test is positive the practitioner should refer the patient at once to the nearest hospital ante-natal clinic or V.D. department. It would seem almost unnecessary to mention this were it not known of instances where the general practitioner has done nothing further regarding a positive blood test.

Prompt and adequate therapy

Syphilis in pregnancy having been diagnosed as early as possible (as has been outlined previously) prompt and adequate therapy should be given. In the days of arsenic and bismuth, inadequate therapy was one of the factors responsible for the occurrence of congenital syphilis.

Inadequate therapy should not now be a problem as an adequate course of antisyphilitic treatment can be given in the form of penicillin in a short time - 5-10 million units in 10 days. With co-operation of the patient a single daily injection of $\frac{1}{2}$ to 1 million units for 10 days can be administered at the V.D. outpatient department. If there is any likelihood of the patient being delinquent, then she should be admitted to hospital for treatment.

The case for a second course of penicillin in latent syphilitic mothers treated early in pregnancy in view of an occasional syphilitic infant occurring has already been discussed (p.20)

If there is clinical and/or serological relapse of early syphilis later in pregnancy, then therapy has obviously been inadequate and further treatment should be given.

Careful follow-up.

Once treatment has been given there should be regular follow-up (clinical and serological) to note the course of the disease. Although penicillin has given greatly improved results it is not uniformly successful, particularly in cases treated late in pregnancy - and it certainly has not removed the need for careful follow-up in the ante- and post natal periods - stated.

Close collaboration between Venereologist and Obstetrician

In medical conditions complicating pregnancy, best results have been obtained when there is close collaboration between the medical and obstetrical departments. I have the impression that close team work is not always present in syphilis complicating pregnancy.

It has been found in some instances that the patient may attend for ante-natal care but not attend the V.D. department for surveillance. It would be a satisfactory arrangement if these syphilitic patients could attend for ante natal care on the same day and be seen then by the venereologist in a room set aside for the purpose in the ante natal clinic. This is actually done in some well organised clinics.

Also on delivery of the infant, the venereologist should be informed so that treatment and/or surveillance can be supervised from the earliest moment. Syphilitic infants may be weakly and are very prone to infections such as gastroenteritis and broncho-pneumonia. Therefore, there should also be close collaboration with the paediatrician.

The achievement of the above factors would result in really adequate ante-natal care and with prophylactic treatment in any doubtful case, congenital syphilis could be practically eliminated.

The cases reviewed in this series were delivered in the Maternity Department, West Middlesex Hospital, Isleworth, Middlesex.

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S U M M A R Y

- (1) 152 cases are presented for review and discussion under 4 clinical groups.
- (2) A total of 102 cases of acquired (early or latent) syphilis is available for study, including treated and untreated. There were 20 unsuccessful outcomes (late abortions, still-births, and death up to 6 weeks) and in 12 of these congenital syphilitic changes were present. 10 infants were diagnosed as congenital syphilis (but 3 may not have been) These figures are not good, and are obviously capable of improvement.
- (3) (i) 74 cases were treated with penicillin.
7 cases of live congenital syphilitic infants occurred (including the 3 above)
In 7 unsuccessful outcomes 3 showed evidence of syphilis. Thus, 7 out of 74 were definitely syphilitic - an incidence of 9.5%. This is much higher than that obtained in some American series, where the incidence given is 1-2%. Yet this is the lowest possible figure, and is probably higher because:-
 - (a) Some, or all of the remaining 7 may have been syphilitic.
 - (b) 23 out of 67 defaulted.
- (ii) If treated before 28 weeks results are satisfactory, particularly in early syphilis. There was no case of congenital syphilis in this group. However, 2 definite cases of congenital syphilis resulted where the mother was treated for latent syphilis early in pregnancy.
- (iii) Treatment after the 28th week gave disappointing results. In early syphilis only 4 out of 8 infants survived.

In 17 latent syphilitic patients there were 5 infants treated for congenital syphilis, 1 neo-natal death and 1 still-born infant.

It is therefore evident that congenital syphilis is still occurring despite penicillin therapy given in what is generally accepted as adequate dosage. Even with the introduction of this powerful anti-spirochaetal agent the need for early attendance of the ante-natal patient, early diagnosis, adequate therapy, careful follow-up, ante-natally and post-natally is as great today as ever.

These factors are necessary for really satisfactory results.

- (4) The results to infants of mothers not treated prior to delivery are disastrous. Infants of such mothers should be treated as congenital syphilis.
- (5) 16 congenital syphilitic mothers were treated during pregnancy. 34 women were treated prior to pregnancy and most received prophylactic treatment. In these 50 pregnancies no case of congenital syphilis occurred. These results were as expected.
- (6) In view of :-
 - results in present series
 - difficulty in interpretation of serology at birth
 - high default rate - a very important factora basis for treatment has been suggested and detailed.
- (7) There should be close collaboration between venereologist, obstetrician, and paediatrician. It is felt there is room for improvement in ante- and intra-natal care (1 maternal death) of the syphilitic woman. It may be stressed that every pregnant woman should have a Wassermann and Kahn test at the first visit.
- (8) With the achievement of the factors mentioned at the end of para 3, and in para 7, there would be great improvement in the figures reported in this series. Also with the prophylactic treatment of any doubtful case, the incidence of congenital syphilis could be practically eliminated.