CONGENITAL SYPHILIS

A STUDY AT PROVINCIAL HOSPITAL

UITENHAGE

A Esselaar

A dissertation submitted to the Department of Paediatrics and Child Health of the University of Cape Town in partial fulfilment of the requirements for the degree M.Phil in Maternal and Child Health.

September 1998
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Signed by candidate
signature removed

SIGNATURE

DATE
ACKNOWLEDGEMENTS

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Sr L de Lange and Staff of the Maternity Ward.

Sr V Doyle & Staff of the Paediatric Ward.

Mr O Bosch and Staff at SAIMR Uitenhage.

Mr S Hlaka and Staff at Record Department Provincial Hospital.

My six children for their loving encouragement.
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<tr>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>ANC</td>
<td>Antenatal Clinic</td>
</tr>
<tr>
<td>Booked</td>
<td>Patient attended antenatal clinic on at least one occasion</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control, Atlanta Georgia</td>
</tr>
<tr>
<td>CPA</td>
<td>Cape Provincial Administration</td>
</tr>
<tr>
<td>EPBTS</td>
<td>Eastern Province Blood Transfusion Service</td>
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<tr>
<td>FTA-ABS</td>
<td>Fluorescent Treponemal Antibody Absorption Test</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immune Virus</td>
</tr>
<tr>
<td>LA</td>
<td>Local Authority</td>
</tr>
<tr>
<td>MOU</td>
<td>Midwife Obstetric Unit</td>
</tr>
<tr>
<td>PEP</td>
<td>Perinatal Education Programme</td>
</tr>
<tr>
<td>PHU</td>
<td>Provincial Hospital Uitenhage</td>
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<tr>
<td>PNMR</td>
<td>Perinatal Mortality Rate</td>
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<tr>
<td>PPIR</td>
<td>Perinatal Problem Identification Programme</td>
</tr>
<tr>
<td>RPR</td>
<td>Rapid Plasma Reagin Test</td>
</tr>
<tr>
<td>SAIMR</td>
<td>South African Institute for Medical Research</td>
</tr>
<tr>
<td>SANCO</td>
<td>South African National Civic Organisation</td>
</tr>
<tr>
<td>STD</td>
<td>Sexually Transmitted Disease</td>
</tr>
<tr>
<td>TPHA</td>
<td>Treponema Pallidum Haemagglutination</td>
</tr>
<tr>
<td>Unbooked</td>
<td>Patient did not attend antenatal clinic</td>
</tr>
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ETHICAL ISSUES

1. Permission was obtained from the Medical Superintendent at Provincial Hospital Uitenhage for use of records.

2. Patients' names are known only to the investigator: records are identified by study numbers.

3. Results will be made known to the Staff at Provincial Hospital and at Laetitia Barn Midwife Obstetric Unit, Kwanobuhle.
ABSTRACT

Aims

1. To establish the extent of Syphilis in Pregnancy and the association of syphilis with unbooked status and perinatal deaths.

2. To determine why the diagnosis was not made in forty cases of Early Congenital Syphilis.

Objectives

1. To establish the percentage of patients with syphilis at delivery and possible association between unbooked status and positive syphilis serology.

2. To determine the Perinatal Mortality Rate and establish what percentage of perinatal deaths occurred in unbooked patients and in those with positive syphilis serology.

3. To establish booking status, place of delivery, whether treated or not, serological findings, signs and symptoms of infants with Early Congenital Syphilis.

Study Design


Setting

Maternity and paediatric wards at Provincial Hospital Uitenhage, East Cape.

Patients and Methods

1. Records were studied of 154 maternity patients delivering in March 1994 in order to ascertain booking status and serology results.

2. Data on sixty-one perinatal deaths weighing over 500 grams was examined to establish maternal booking and serological status.

3. Folders of forty patients with Early Congenital Syphilis admitted to the paediatric ward were examined.

Results

1. Syphilis in Pregnancy :
   i) Prevalence of syphilis at delivery was 9% for patients with titres $\geq 1:8$.
   ii) Unbooked patients totalled 47% of deliveries (73/154).
   iii) Fifteen percent of deliveries had no syphilis serology tests performed and were discharged without screening (23/154).
   iv) No significant association was found between unbooked status and positive serology (p=0.35).

2. Perinatal Deaths :
   i) In instances of a perinatal death, a significant association was found between unbooked status and positive RPR serology (p=0.017).
   ii) Perinatal death rate due to syphilis totalled 10.8/1000 deliveries.
3. Early Congenital Syphilis:

i) Eighty-five percent of cases (34/40) delivered at PHU and were mismanaged by personnel.

ii) Eighteen of the thirty-four mothers had attended antenatal clinic and were untreated or inadequately treated by the time of delivery (53%).

iii) Sixteen of the mothers had been unbooked and were discharged without screening or treatment (47%).

iv) Four booked patients had negative serosurveillance during the antenatal period.
Conclusion

Provincial Hospital Uitenhage serves a poor community. This is reflected in the high prevalence of syphilis at delivery and the high proportion of unbooked patients.

Time-consuming and inefficient methods of serosurveillance plus separate clinics and staff for antenatal and Sexually Transmitted Diseases compounded existing problems.

The standard of care anticipated at a Level 2 Referral Hospital was not delivered by Health Workers, largely due to lack of in-service training and guidelines for the management of Syphilis in Pregnancy.

Recommendations

1. In-service staff training by the Perinatal Education Programme (PEP) and adoption of protocols of management.

2. Rapid ("same-day") availability of serology results and initiation of treatment at Antenatal Clinic.

3. RPR at booking visit and repeated at delivery in all patients.

4. Monthly evaluation by Perinatal Problem Identification Programme (PPIP) and Obstetric/Paediatric meeting to monitor implementation.
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1. INTRODUCTION AND LITERATURE REVIEW

1.1 In April 1994 the Development Bank of Southern Africa published a paper setting out various socio-economic indicators pertaining to the nine Provinces of South Africa. The Eastern Cape was shown to have the highest Infant Mortality Rate (58.2/1000 live births) and the second lowest Income per Capita (R1,358 per annum) in South Africa. (1)

Set in the western half of the Eastern Cape, Uitenhage has one hospital maternity unit - the Provincial Hospital (PHU) and one Midwife Obstetric Unit (MOU). These serve a population of 250 000 people (See Appendix 1). Approximately 3,500 deliveries are performed annually at these two units, and about 25% of them at MOU.

1.2 A number of studies throughout South Africa on societies with similar backgrounds, have demonstrated that syphilis constitutes a significant health problem:

At King Edward VIII Hospital, Durban in 1983, active syphilis was diagnosed in 7.4% of mothers who delivered. (2) The Perinatal Mortality Rate due to Congenital Syphilis at this hospital in 1978 was 3.2/1000 deliveries. (3)

Unbooked maternity patients at delivery tested Rapid Plasma Reagin (RPR) positive in 9.6% of cases and booked patients were RPR positive in 1.8% of cases in a study at Baragwanath Hospital in 1985-6. (4)

Groote Schuur Hospital had a figure of 7.6% of patients at antenatal clinics testing positive for syphilis in a 1985 study. (5)

A study at Kalafong in 1987, found that 10.5% of the Perinatal Deaths were due to Congenital Syphilis. (6)

In an unpublished report at Cecilia Makiwane Hospital, East London (1992), syphilis was diagnosed in 14.5% of patients at antenatal clinic. 18.1% of the
unbooked cases screened positive for syphilis. (Personal Communication - Mary Mathai and Sue Harris).

In Khayelitsha in 1992, 12.5% of booked cases were VDRL positive as were 32.3% of a small number of unbooked cases. (7)

In 1993 at Johannesburg Hospital, 4.7% of deliveries had positive RPR screening tests. These cases were found to have significantly higher rates of incomplete abortion and stillbirth than the total obstetric population. (8)

In 1994 a study at Tygerberg Hospital of Perinatal Deaths weighing over one kilogram, showed that the rate in 1984 was 27/1000 deliveries, and dropped to 21 in 1993. 15% of stillbirths were due to infection, with syphilis causing more than half of the infections. Although only 4.7% of patients were unbooked, they accounted for 42% of all stillbirths. (9)

1.3 For over a decade, recommendations have been made to resolve the problem of Syphilis in Pregnancy and Congenital Syphilis. These include:

1.3.1 Screening at first antenatal visit, third trimester and at delivery in "High Risk" populations

Although the incidence of venereal syphilis declined dramatically in developed countries after the introduction of Penicillin in the 1940's, the situation in Africa in the 1990's does not demonstrate a similar improvement. Very high rates of venereal syphilis are found in urban areas in many African countries, as well as high rates in pregnancy and high incidences of Congenital Syphilis. (10) Prevalences of syphilis seroreactivity in pregnant women attending antenatal clinics in Africa range from 4% to 15%. (3.5.6.10.17.20.21) These findings are consistently high and may even be underestimates. All health workers in Africa especially those concerned with maternal and child care, must be aware that syphilis on this continent has a prevalence similar to that of the pre-antibiotic era. Screening and early treatment of pregnant women is therefore essential in order to reduce perinatal morbidity and mortality. (10)
1.3.1.1 A study in Zambia in 1982 by Ratnam and colleagues, (11) found that 12.5% of antenatal attenders had positive Treponema Pallidum Haemagglutination (TPHA) Tests, as did 42% of women with stillbirths. More than 8% of all infants under three months admitted to the wards, had Congenital Syphilis. They discovered that:-

i) Patients with a non-reactive test result for syphilis in early pregnancy had seroconverted by the time of delivery, thus highlighting the inadequacy of a single serological test. Seroconversion occurred by the time of delivery in ten (3.7%) of the 269 patients who had had non-reactive tests early in pregnancy;

ii) Although 85% of pregnant women attended antenatal clinics, only about one quarter had been screened for syphilis by the time of delivery;

iii) In the study of 464 women admitted for delivery, they found that only eleven out of the fifteen patients with positive VDRL test at booking visits, had received treatment by the time of the delivery;

iv) Six percent (30 out of 470 infants deliveries) of neonates had reactive serological tests - RPR and TPHA were positive. Of these thirty babies, sixteen were healthy, two were stillborn, four were symptomatic and a further eight required intensive care for prematurity and asphyxia.

v) Babies born to women who had not sought antenatal care were at high risk for Congenital Syphilis. VDRL testing of 68 women who did not attend antenatal clinic revealed that eight (12%) tested positive for syphilis compared to 7.5% in booked patients (40/264).

The authors therefore recommended:-

- screening tests be performed when pregnancy confirmed;
- repeat screening to detect cases of seroconversion and infection acquired later in pregnancy;
babies born to women not attending antenatal clinic were at risk for congenital syphilis and should be tested;

women not attending health services for antenatal care and/or delivery should have their infants screened as soon as possible.

1.3.1.2 The dramatic 240% increase in cases of Congenital Syphilis in New York City in 1985, led to the Centers for Disease Control (CDC) recommending screening at the initial visit, in the third trimester and at delivery, in high-risk areas.

They also recommended that infants should not be discharged until screening results are known, and that screening tests be performed on the mother's blood not on cord blood. (12)

False negative and false positive results can occur with cord blood specimens. Contamination with Wharton's jelly may cause false positives; infection acquired late in pregnancy may lead to false negative results on cord blood. (22)

1.3.1.3 In 1993 Opai-Tetteh and colleagues at King Edward VIII Hospital Durban, found a screening test positive rate of 11% at the initial visit and that a further 3% of patients were positive by the time of delivery. Owing to the high cost of the CDC proposal, they suggested screening at the initial visit and at delivery in high-risk areas. (13)

1.3.2 On-site screening at all clinics in order to diagnose and treat positive cases immediately and reduce attrition rates

On-site screening was initiated in 1986 by Delport at Kalafong. Having results available immediately meant RPR positive patients' treatment was commenced there and then. The "Card Test" used compared well with the Central Laboratory results and had a sensitivity of 83.3% and specificity of 99.8%. (14,29)
Swingler and de Groot, in Khayelitsha in 1992, performed a study examining the efficiency of the system for antenatal prevention of congenital syphilis. They identified two main problems - viz; delay in results reaching the clinics as the laboratory was centralized, and the high rate (24.5%) of attrition of patients referred to separate Sexually Transmitted Diseases (STD) Clinics in the same building. (7) They postulated that on-site screening would lead to earlier treatment and eliminate the necessity of tracing patients who required treatment. The difficulty of maintaining quality control in nine peripheral MOU "laboratories" would have to be overcome.

1.3.3 The high-risk "unbooked" patient

1.3.3.1 A study at Baragwanath Hospital in 1989 showed that 25% of 9000 cases screened were unbooked. Ten per cent of the unbooked as opposed to 1.8% of the booked cases had RPR titres equal to or more than $1 : 8$. Forty-one infected infants born in the study period were all delivered of unbooked mothers. (4)

1.3.3.2 In 1990 Mlisana and colleagues at King Edward VIII Hospital studied a series of 114 mothers with no previous history of antenatal care. Thirty-one per cent of these cases had positive RPR tests. Fifty-nine per cent of the RPR titres were equal to or more than $1 : 8$. Symptomatic neonates were born to four mothers, all of whom had titres of $1 : 16 - 1 : 32$. (15)

1.3.3.3 Meyer and Malan at Groote Schuur Hospital, in a prospective study in 1989, concluded that unbooked status was a predictive factor for the development of Congenital Syphilis ($p=0.036$). They followed up (for 3-4 months), sixty-six infants delivered to VDRL positive mothers who had untreated or inadequately treated syphilis. Fourteen of the fifteen infants with Congenital Syphilis were born to untreated mothers.
1.3.4 Notification of Congenital Syphilis

In February 1991 the disease was made notifiable in South Africa to increase awareness by Health Workers, and obtain accurate data for analysis. Ballot and Rothberg's study (8) shortly after the disease was made notifiable (May 1991 - April 1992), found that at Johannesburg Hospital, only 12% of cases were actually notified. In 1993 a survey, also by Ballot and Rothberg (17) of nine teaching hospitals showed that, whilst consensus exists as to the need to notify symptomatic cases, confusion reigned when it came to the asymptomatic cases. The authors suggested that all cases which fulfilled the CDC criteria (32) needed to be notified, and scrupulous record-keeping should be insisted upon, to avoid unnecessary treatment of infants whose mothers have already been fully treated.
2. MOTIVATION

The regular admission of cases of Early Congenital Syphilis each year prompted further investigation of the reasons for the diagnosis being missed at delivery. It was anticipated that most of these patients would have been born to unbooked mothers, unbooked status being considered as a major problem in the prevention of Congenital Syphilis.

The unexpected discovery that the majority (34/40) of the children with Congenital Syphilis had been delivered at PHU and that less than half of the cases were unbooked, led to further probing to uncover all areas where "missed opportunities" for preventing Congenital Syphilis could have occurred. It therefore became important to determine the prevalence of syphilis in patients in the maternity wards and the perinatal mortality from the disease. Reasons for failure to prevent Congenital Syphilis needed to be determined.
3. **AIMS**

3.1 To establish the extent of the problem of Syphilis in Pregnancy and its "possible association" with unbooked status and with perinatal deaths;

3.2 To determine the reasons why the diagnosis was not made at or before delivery, in forty cases of Early Congenital Syphilis admitted to the paediatric ward.

4. **OBJECTIVES**

4.1 To establish what percentage of women at delivery tested positive for syphilis and if there was a significant association between unbooked status and positive serology.

4.2 To determine the Perinatal Mortality Rate at Uitenhage Provincial Hospital and to establish what percentage of perinatal deaths occurred in unbooked patients and in those with positive syphilis serology.

4.3 To establish maternal booking status; place of delivery; whether or not treatment of the mother was initiated either antenatally or at delivery; the maternal and neonatal serological findings; presenting signs and symptoms of neonates with Early Congenital Syphilis; and whether the newborn baby received any treatment after delivery.
5. PATIENTS & METHODS

5.1 Problem of Syphilis in Pregnancy

Prompted by the number of admissions to the hospital of children with Early Congenital Syphilis, an attempt was made to identify areas of "missed opportunity" for diagnosing and treating syphilis in the mother.

5.1.1 A retrospective study of all patients admitted to the labour ward during the month of March 1994 was undertaken to establish their booking and RPR status. This month was chosen for convenience. The findings were not expected to differ from those of any other month.

5.1.2 The RPR status and booking status of each patient was looked for in the patients' folders, antenatal clinic records, ward record and the labour ward birth register. SAIMR computer records were resorted to for RPR status, if results were not forthcoming. If no records were available, it was assumed that the blood specimen had not been sent.

Private patients were excluded from the study as the majority had no record of RPR status in their hospital files. These private patients were booked and delivered by private practitioners, who did not make their patients' RPR status known to hospital staff, if indeed this test was done.

5.1.3 The number of mothers testing positive was determined and the relationship between booking status and syphilis serology determined, using the chi-square test on 2x2 tables on the Epi-Info computer programme.

5.1.4 Laboratory Tests

Serology results were supplied by the Eastern Province Blood Transfusion Services (EPBTS) in Port Elizabeth, thirty kilometres away. This laboratory processed all routine antenatal bloods specimens for group Rh and RPR. Blood was taken at the patient's booking visit, and patients requested to return in one or two weeks for the results. Result slips were then stapled to the patient-held ANC card.
In cases where patients were unbooked or had no record of results from EPBTS in their folders, blood was taken at delivery (in some instances). This blood was sent from the labour ward to the South African Institute for Medical Research laboratory (SAIMR) on the premises at Uitenhage Hospital. The results of RPR tests were available on the same day in most instances. TPHA tests were performed on positive specimens at the Port Elizabeth branch of this laboratory, and results were available two days later.

5.1.5 RPR Titres

According to current policy RPR titres $\geq 1:8$ were regarded as positive. (29) The highest titres are generally found in the first year or so of syphilitic infection and start to drop once the latent stage is reached. Primary infection acquired late in pregnancy and latent stage syphilis may present with negative RPR or with titres <1:8. Biologically false positive RPR results have low titres.

The titre of 1:8 was chosen because of Venter's study of 9071 patients at delivery, which found that all of the 41 affected infants were born to mothers with RPR $=$ 1:8. (4) Maternal titres $=$ 1:16 were associated with infants with Congenital Syphilis in Misana's study (15), while more recently Meyer and Malan found that a titre of 1:32 was a predictive factor for the development of Congenital Syphilis.

5.2 Perinatal Deaths

5.2.1 The Perinatal Mortality Rate (PNMR) for this Institution was unknown. The study on "Perinatal Mortality in the Cape Province 1989 - 1991" by Louw, Khan et al, was reviewed as it was the only known source of information of PNMR at this Hospital. The study excluded infants weighing less than 1000 grams, and the Uitenhage area results were incorporated with those of Port Elizabeth.

The PNMR for 1992 - 1994 was calculated by referring to the six-monthly statistic forms submitted to the Cape Provincial Administration in Cape Town. From 1992 this total included all infants weighing 500 grams and more.
5.2.2 PNM: January - June 1995

A prospective study was undertaken of all perinatal deaths over 500 grams for the six-monthly period January to June 1995. This six-month period was chosen for convenience; there was no reason to suspect that the perinatal deaths should differ significantly from any other period. Poor documentation of RPR, booking status and treatment had been noted in patients' records and birth register when looked at retrospectively. It was therefore decided to examine each perinatal death prospectively as soon as possible after death, in an attempt to avoid these shortcomings. Autopsies were not performed.

The relationship between:
- syphilis serology and perinatal death;
- booking status and perinatal death;
- syphilis serology and booking status in perinatal deaths were calculated using Fishers exact test on the Epi-Info computer programme.

5.2.3 Notification of Congenital Syphilis

Since notification of Congenital Syphilis was introduced in 1991, an enquiry was made as to the routine followed in PHU by Ward Sisters when they came across syphilitic stillbirths or newborns.

5.3 Early Congenital Syphilis

5.3.1 Paediatric ward admission records were examined over the period 1.1.1990 - 31.12.1994. All patients discharged with the final diagnosis of Congenital Syphilis were included in the study (Appendix II). The diagnosis of syphilis was made in patients fulfilling the criteria of "Presumptive Syphilis" as laid down by the CDC. (32)

The infants' folders, mothers' folders (if the infant was born at PHU) Labour ward birth register and SAIMR laboratory records were used to find information on booking and RPR status of the mothers, and the syphilis serological status of the infants. The clinical features upon which the diagnosis was made were identified from the infants' folders. The presenting clinical features of Congenital Syphilis in these infants were documented.
Laboratory tests:

In this study, RPR tests (Becton Dickinson) were performed on both infant and maternal specimens, as far as possible. These initial tests were done on site at the SAIMR laboratory Uitenhage. All specimens testing positive were sent to Port Elizabeth SAIMR where TPHA tests (Immu-Trept, Davis Diagnostics) were performed as confirmation. Infant venous blood was tested for Fluorescent Treponemal Antibody Absorption Tests (FTA-ABS), IgG and IgM (Diagnostic and Technical Services).
6. RESULTS

6.1 Problem of Syphilis in Pregnancy

6.1.1 Percentage with positive serology at delivery

6.1.1.1 During March 1994, there were 201 deliveries at PHU and its MOU. Forty-seven were "private" and 154 were hospital cases. One-hundred-and-thirty-one of the 154 hospital cases had documented results of syphilis serology. This constitutes 85% of the patients and is therefore adequate for analysing records in a retrospective study. (30) Patients with titres ranging from 1:2 to 1:256 numbered 25 (19%); 12 cases (9%) had RPR titres \( \geq 1:8 \).

The twenty-three patients whose RPR status was unknown, were discharged without screening. These patients constituted 15% of the 154 hospital deliveries. As they were all unbooked, it could be expected that they had a higher risk of being RPR positive (8,10).

6.1.1.2 The prevalence of syphilis at delivery is high - at least 19% if all titres are considered, and 9% for patients with titres \( \geq 1:8 \).

6.1.2 Association between Syphilis and Unbooked status

6.1.2.1 Seventy-three (47%) of the 154 patients were unbooked and, of these, ten cases tested positive for syphilis, forty were negative, and in the remaining twenty-three patients, RPR status was unknown. Fifty-three percent (81 cases) were booked patients, of which fifteen had positive RPR and sixty-six had negative results.
TABLE I
ASSOCIATION BETWEEN BOOKING STATUS AND SYPHILIS
(ALL TITRES) WHERE RPR STATUS WAS KNOWN
n = 131

<table>
<thead>
<tr>
<th></th>
<th>UNBOOKED n = 50</th>
<th>BOOKED n = 81</th>
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<tr>
<td>RPR+</td>
<td>10 (20%)</td>
<td>15 (18.5%)</td>
</tr>
<tr>
<td>RPR-</td>
<td>40</td>
<td>66</td>
</tr>
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(\textit{p}=0.83) Odds Ratio \(= 1.10\) \((0.41 < \text{OR} < 2.92)\)

There is no significant difference between booked and unbooked patients in their syphilis serology status. This does not take into account the 23 patients in whom syphilis serology was unknown.

6.2 Perinatal Deaths

6.2.1 Perinatal Mortality Rate

The PNMR at Uitenhage Provincial Hospital ranged from 33 to 47/100 deliveries for the years 1991 to 1994. The figure included infants weighing 500 grams and more as from 1992. The average rate for the period was 40/1000.

TABLE II
PNMR

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<th>YEAR</th>
<th>NO. OF PN DEATHS</th>
<th>TOTAL DELIVERIES</th>
<th>PNMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>160</td>
<td>4039</td>
<td>39.6</td>
</tr>
<tr>
<td>1992</td>
<td>173</td>
<td>3695</td>
<td>46.8</td>
</tr>
<tr>
<td>1993</td>
<td>139</td>
<td>3430</td>
<td>40.5</td>
</tr>
<tr>
<td>1994</td>
<td>110</td>
<td>3304</td>
<td>33.3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>582</td>
<td>14468</td>
<td>40.2</td>
</tr>
</tbody>
</table>
6.2.2 PNM : January - June 1995

6.2.2.1 During the six-month period January to June 1995, sixty-one perinatal deaths occurred in 1 291 deliveries at Provincial Uitenhage; thirty-five stillbirths and twenty-six Early Neonatal Deaths. PNMR was therefore 47.2/1000.

6.2.2.2 Unbooked patients and Perinatal Deaths

Ten of the sixty-one patients who had a perinatal death were unbooked (16%), seven had no record of booking status (11%) and forty-four were booked cases. Since more than 80% of cases had known booking status, the findings may be regarded as valid. (30)

6.2.2.3 Maternal Syphilis and Perinatal Deaths

Forty of the sixty-one patients with perinatal deaths tested negative for syphilis (65%), while the RPR was not established in seven cases. Fourteen perinatal deaths (25.9%) were associated with positive maternal serology - eleven of these patients had titres $\geq 1:8$. In one instance, the patient had positive syphilis serology and a perinatal death, but her booking status was not recorded.

This gives a perinatal mortality rate of 10.8/1000 deliveries for infants born to mothers who have positive serological tests for syphilis. This figure would be higher if some of the seven 'RPR unknown' patients proved to be positive. As over 80% of RPR results were known, the findings are acceptable. (30)

6.2.2.4 Maternal Syphilis in Unbooked patients with Perinatal Deaths

Sixty percent of the unbooked patients in whom there was a perinatal death, and 20% of the booked patients; tested positive for syphilis; this is statistically significant ($p=0.017$). Booking status in one of the patients with positive syphilis serology was unknown.
### TABLE III
ANALYSIS OF PERINATAL MORTALITY
WHERE BOOKING STATUS AND RPR STATUS WERE KNOWN

\[ n = 47 \]

<table>
<thead>
<tr>
<th>SEROLOGY</th>
<th>UNBOOKED</th>
<th>BOOKED</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPR+</td>
<td>6 (60%)</td>
<td>7 (20%)</td>
</tr>
<tr>
<td>RPR-</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>TOTAL</td>
<td>10</td>
<td>37</td>
</tr>
</tbody>
</table>

\[ (p=0.017) \text{ Odds ratio} = 6.43 \ (1.16 < \text{OR} < 38.77) \]

A statistically significant association was found between unbooked patients with positive syphilis serology and perinatal deaths \( (p=0.017) \).

#### 6.2.3 Notification of Congenital Syphilis

Notification slips were completed by Ward Sisters, signed by the Doctor and collected by the porter and taken to a central point for collection by the Municipality. It was found that each ward had 2 or 3 partially completed notification books. Some contained notification slips dated months previously and not yet signed, or signed and not torn out for dispatch to the Municipality.

All the staff were extremely vague as to the criteria for notification. CDC protocols of management were not employed (32) and constant rotation of different doctors through the department left no dedicated person with whom to consult. Direct questioning of the sisters revealed that only the obviously symptomatic cases of Congenital Syphilis were notified, while stillbirths had never been considered as notifiable. These findings confirm those in the study by Ballot and Rothberg (7).
6.3 Early Congenital Syphilis

There were forty Early Congenital Syphilis admissions to the hospital during the period 1990 - 1994. Thirty-four of these forty babies who fulfilled the criteria of "Presumptive Syphilis" of the CDC (32) were born at PHU. Only twenty-two of the thirty-four maternal folders could be traced. Most of these folders had data missing, including treatment received. In instances where folders were not found, a limited amount of information regarding the mother was obtained from the baby's folder, labour ward Birth Register and SAIMR laboratory. Data relating to the study of admissions with Early Congenital Syphilis was divided into maternal, infant and serological.

6.3.1 Maternal Data

6.3.1.1 Maternal ages ranged between 16 and 27, with the mean age of 20 years.

6.3.1.2 Eighteen (45%) of the mothers of the forty affected infants had attended ANC at least once. Nineteen patients (47%) were unbooked and in three cases, the booking status was unknown.

6.3.1.3 Thirty-four of the forty cases (85%) delivered at PHU or its MOU, three had home deliveries and three were from other hospitals.

<table>
<thead>
<tr>
<th>TABLE IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPR STATUS AND BOOKING STATUS</td>
</tr>
<tr>
<td>OF PATIENTS DELIVERED AT PHU</td>
</tr>
<tr>
<td>n = 34</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SEROLOGY</th>
<th>UNBOOKED</th>
<th>BOOKED</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPR+</td>
<td>16 (47%)</td>
<td>14 (41%)</td>
</tr>
<tr>
<td>RPR-</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

(p=0.065) Odds Ratio Undefined

There is no significant association between unbooked status and positive RPR serology (p=0.065). Thirty of the thirty-four mothers delivered at PHU were known to be RPR positive at or shortly after delivery.
6.3.1.4 Booked Cases

Despite having attended ANC at least once, fourteen of the eighteen booked cases (77%) who tested positive for syphilis, either received no treatment at ANC (9 cases), or were inadequately treated (5 cases). After delivery the infants of these fourteen mothers received no treatment and were discharged home with their mothers the following day. Four of the eighteen however, were PRP negative at booking, so that syphilis was not suspected at delivery.

i) Booked and Inadequately Treated

Three of the five inadequately treated patients had poor records relating to dates of attendance and dates of treatments given for positive serology. In the other two patients, Case 37 (Appendix II) was a 16-year-old primip who receive an injection of Benzyl Penicillin on the day before she delivered - her first visit to ANC. Case 39 was a teenager with an RPR titre of 1:512. She made her booking visit eleven days before the infant was born and treatment was initiated on that day. In all these instances the mothers and babies were discharged without any treatment given to either by the attending Maternity Ward staff.

ii) Booked and Untreated

Nine of the patients who attended ANC were untreated by the time of delivery. It was recorded in the patient's files that RPR was positive at ANC, but no treatment was given to either mother or baby in cases 30 (RPR 1:128) and 31 (RPR 1:32) (Appendix II). The Birth Register comment in Case 18 states "RPR positive, but not yet treated, according to the patient". The patient in question was referred from Regional Services and documented as having an RPR titre 1:8 but not treated at ANC. In the instance of Case 40, the teenage parents, both scholars, were fully treated after the birth of the baby - who was not treated. The mother's first visit to the ANC was two weeks prior to delivery.
iii) Booked and RPR Negative at Antenatal Clinic

Folders of two of the four patients with negative serology at ANC were traced. Case 19 was a 17-year-old primip who reported for booking at twenty-six weeks gestation and had a negative RPR. She attended ANC four times. Her infant presented at the age of three months with a titre of 1:512. Case 20 had negative serology at her booking visit at twenty-four weeks and attended ANC seven times. RPR was only repeated two weeks after delivery when the patient developed sepsis after a Caesarian Section.

6.3.1.5 Unbooked Cases

All of the sixteen unbooked patients (47% of the cases) were discharged without screening for syphilis, and the babies had received no treatment on discharge.

In certain cases, the Health Worker had noted in the folder "Non-Clinic case (meaning unbooked), bloods taken", but the patient was discharged before the results were known. "RPR positive, per phone, titre to follow" was recorded in another (Case 15) but no action was taken.

The 16-year-old unbooked Gravida 2 (Case 28) had an RPR titre of 1:256 at delivery and she was sent home without treatment. The baby's titre two weeks later was 1:4096.

Almost 50% of the mothers of infants with Early Congenital Syphilis had never attended antenatal clinic. Despite this, they were discharged from PHU without screening of treatment.

Just over half of the mothers of these infants had attended ANC and had received no treatment or inadequate treatment by the time of delivery. They were neither screened nor treated at delivery at PHU.
6.3.2 Neonatal Data

Nineteen babies presented between the ages of 7 and 30 days, ten between 31 and 90 days, and eleven were more than 90 days old. The most important presenting symptoms were rash (45%), snuffles, jaundice, painful limb and gastro-enteritis. The commonest signs were rash, fever, radiological changes in the long bones, rhinitis, anaemia, hepatosplenomegaly and pseudoparesis. See Appendix II.)

Most infants presented under the age of three months and had multi-system disease. Three of them are known to have died (a mortality rate of 7.5%), one of whom was born to a mother known to be Human Immune Deficiency (HIV) positive. One case of Syphilitic Nephrosis was diagnosed and one had severe Haemolytic Anaemia. Cerebrospinal fluid (CSF) studies were only performed in one case which presented with opisthotonos and was transferred to Livingstone Hospital. No record of the CSF results was found in the folder.

6.3.3 Serological Data

TABLE V
FREQUENCY DISTRIBUTION OF MATERNAL AND NEONATAL TITRES

<table>
<thead>
<tr>
<th>Reagin Titres</th>
<th>Maternal Titres</th>
<th>Neonatal Titres</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>0.0</td>
<td>0.5</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Syphilis serology on both mother and baby was performed where possible, on admission of the baby to the Paediatric ward. In nineteen of the cases the maternal titres were equal to or greater than 1:16. Nineteen of the infants with records of titres in the folder, had RPR titres equal to or greater than 1:8.

FTA-ABS tests were recorded in twelve infants with titres ranging from "positive" to 1:4096.

<table>
<thead>
<tr>
<th>PATIENT NO.</th>
<th>RPR TITRE</th>
<th>FTA-ABS TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Units IgG</td>
<td>IgM</td>
</tr>
<tr>
<td>1</td>
<td>512</td>
<td>3 Borderline</td>
</tr>
<tr>
<td>2</td>
<td>128</td>
<td>3 1</td>
</tr>
<tr>
<td>19</td>
<td>512</td>
<td>4 3</td>
</tr>
<tr>
<td>28</td>
<td>4096</td>
<td>4 4</td>
</tr>
<tr>
<td>31</td>
<td>64</td>
<td>3 3</td>
</tr>
<tr>
<td>34</td>
<td>1024</td>
<td>2 2</td>
</tr>
<tr>
<td>36</td>
<td>Positive</td>
<td>Minimal</td>
</tr>
<tr>
<td>37</td>
<td>Positive</td>
<td>Minimal</td>
</tr>
<tr>
<td>38</td>
<td>64</td>
<td>Strong</td>
</tr>
<tr>
<td>40</td>
<td>64</td>
<td>Strong</td>
</tr>
</tbody>
</table>

Methods of testing and reporting IgG and IgM changed over the years of the study.
7. LIMITATIONS

It is a retrospective study relying on chart reviews with the problems of missing records and information. This was overcome by referring to several other possible sources of information - folders, Labour Ward Birth Register and SAIMR laboratory computer records. However, as indicated in the relevant sections, more than 80% of records were found, which is acceptable.

It would have been useful to have done the whole study over the same period of time, but practical considerations prevented this. However, there is no reason to suspect that there had been any change over the whole period of investigation, as the management of syphilis had remained the same during these periods.

This is a hospital-based study (more specifically a Level 2 Referral Hospital), and results may not necessarily be applicable at other centres in South Africa.
8. DISCUSSION

8.1 Syphilis in Pregnancy

The overall prevalence of known positive syphilis serology at delivery was found to be 19%. Patients with titres ≥ 1:8 were present in 9% of all deliveries, i.e. one in every eleven patients. The study confirmed that syphilis is widely prevalent and constitutes a major problem in pregnancy.

Compared to other centres with patients of similar socio-economic standing, King Edward VIII Hospital had an overall prevalence of 23% (2), whilst other major urban centres had figures closer to the 9% figure at PHU. (5,7,13)

There was no statistically significant difference at PHU between unbooked and booked patients with positive syphilis serology (p=0.35). Figures were high in both categories. This is a surprising finding and is contrary to the findings of other centres. At Baragwanath, Venter found unbooked patients five times more likely to be RPR positive than booked patients. (4) In Swingler's Khayelitsha study, 11.6% of booked patients had positive serology compared with 32.3% of unbooked. (7) Mlisana's study in Natal found the prevalence of syphilis in the unbooked to be 31%. (15)

The study identified another problem area - the discovery that an alarming 47% of patients were unbooked. This figure is appreciably higher than at other centres. Unbooked patients accounted for 24.5% of deliveries at Baragwanath Hospital, (4) 19% at Johannesburg General (8) and only 5% at Khayelitsha MOU. (7) Reasons for non-attendance at ANC were identified by Loening and Broughton. (18) These included ignorance, inaccessible clinics, financial problems, lack of fixed abode and unsympathetic Health Workers at clinics. In this region, clinics are all within easy reach; antenatal care has been free of charge since June 1994, but there are large areas of densely populated informal housing.
The obvious major difference between the Centres quoted above and this Centre is that this is a Level 2 Referral Hospital. A similar study undertaken at another level 2 Referral Hospital in the Eastern Cape may serve to confirm the high level of unbooked patients.

Apart from the high percentage of unbooked patients, the study also revealed that 15% of booked patients (23/154) had no syphilis serological results and were discharged without treatment. This finding has not been commented on by other authors except for Mathai and Harris in their unpublished study at Cecilia Makiwana Hospital in 1992. They write "no result could be traced in 8.6% of 751 deliveries, suggesting that, not only had they not had serosurveillance during their pregnancy, but had also escaped it after delivery" (Personal Communication). As with the unbooked patients, a similar study in another Level 2 Referral Hospital might reinforce the findings at PHU. It is significant that Cecilia Makiwana Hospital is also based in the Eastern Cape - about 300 kilometres from Uitenhage.

In summary:-

i) the prevalence of syphilis at PHU is high;

ii) the rate of unbooked patients is high;

iii) there is no significant difference in RPR rates between booked and unbooked patients;

iv) a high percentage of booked patients without RPR results were discharged without results or treatment.
8.2 Perinatal Deaths

8.2.1 Maternal Syphilis and Perinatal Deaths

It is recognised that syphilis is a common cause of Perinatal Mortality in developing countries. (8,11,15,18,20) This association is confirmed in this study where the PNM associated with maternal syphilis was 10.8/1000 deliveries.

In their Perinatal Mortality Study of the Cape Province in 1989 to 1991, Louw et al (28) targeted the PNMR of the Port Elizabeth-Uitenhage area as one in which "further studies are needed to document the causes and plan appropriate intervention policies". This Port Elizabeth-Uitenhage region had a PNMR of 40.33/1000 - the second highest in the former Cape Province. The stillbirth rate was amongst the highest, despite an "intermediate" Low Birth Weight Rate. The authors (28) comment that, although the causes of the stillbirths are not documented, they "probably include placental abruption and syphilis". The latter is substantiated in the Uitenhage area by this study.

Patients with positive syphilis serology were associated with 25.9% of perinatal deaths. At another East Cape Hospital, Cecilia Makiwana in East London, the rate was 23.4% (Personal communication, Dr Mary Mathai). Similar rates were described at Khayelitsha. (7) Delport reports that at Baragwanath the rate was 2.8%, at Groote Schuur 7% and Kalafong 10.5% - all appreciably lower than the PHU figure. Syphilis is therefore a major factor associated with perinatal death in Uitenhage.

8.2.2 Maternal Syphilis in unbooked patients and the association with Perinatal Deaths

Results of this study confirm that a statistically significant association exists between unbooked status and perinatal deaths in mothers with positive RPR serology (p=0.017). Sixty percent of the unbooked patients who had perinatal deaths had positive RPR results and 20% of booked patients with perinatal deaths tested positive. Venter's study at Baragwanath Hospital (4) showed that the unbooked patient with RPR titre $\geq 1:8$ was at risk of delivering an affected infant. His study demonstrated that unbooked mothers were five times more likely to have positive serology than booked patients.
In their study of 209 seropositive patients at delivery, Ballot and Rothberg (8) found that 133 (63%) of the patients were unbooked. Incomplete abortion accounted for 8 (6%) of their pregnancies in contrast to a rate of 1.97% incomplete abortions for the total obstetric population during the same period. They caution however, that it is not certain if the abortions were all spontaneous or due to interference in the pregnancy.

Delport noted that, despite an attendance rate of 93% at ANC at Kalafong, 38% of patients who had not had syphilis serology done (i.e. they could be regarded as unbooked), lost their babies as a result of Congenital Syphilis. (6)

In all of the studies, positive syphilis serology is associated with a higher perinatal mortality.

An interesting outcome of this investigation is that although there is a high "unbooked" rate at delivery, there is not an increased prevalence of syphilis in the unbooked mothers. However, when there is a perinatal death, there is a significant relationship with positive syphilis serology in the mothers who are unbooked.

8.2.3 Notification of Congenital Syphilis

The problems encountered at PHU were not unique, as illustrated by Ballot and Rothberg (8,17). The staff, including doctors, obviously lacked any protocols of diagnosis and treatment of Congenital Syphilis, and failed to take cognisance of the importance of accurate notification statistics for the Hospital.

The CDC guidelines (32) were found to be complicated and staff were especially confused by the distinction between "confirmed" and "presumptive" cases. The result was that these criteria were largely ignored and probable cases not notified.
8.3 Early Congenital Syphilis

In analysing reasons why the diagnosis was missed in the forty cases admitted as Early Congenital Syphilis, the "missed opportunities" within the hospital provided important clues. Patients with documented positive syphilis serology at antenatal clinic were inadequately treated or not treated by the time that they delivered. After delivery these patients were not investigated further, and neither mothers nor infants were treated as required. Maternal record-keeping at delivery indicated that scant attention was paid to serosurveillance of the patients and seemingly no effort was made to ensure that all patients who were unbooked were investigated and treated, along with their infants.

The problem of the asymptomatic neonate compounded the whole problem and added to the likelihood of missing the diagnosis of Congenital Syphilis.

8.3.1 Maternal Data

The Early Congenital Syphilis study highlighted several points:-

i) The fact that 85% of the cases had delivered at a Level 2 Referral Hospital, where one would anticipate a certain level of competence amongst Health Workers. In these patients, the Health System failed to deliver.

ii) Forty-seven percent (16/34) of mothers of the babies who had Congenital Syphilis were unbooked and yet they were discharged without screening. These 16 patients should not have been discharged without the staff having documented RPR status, initiated treatment, notified and referred for follow-up at STD clinic, with contacts, where applicable. The recent study by Meyer and Malan highlights unbooked status as a predictive factor for Congenital Syphilis (16) and reports throughout the country in different centres confirm the finding. (4,8,15,18)
Apart from the unpublished study by Mathai and Harris, no other authors indicate that unbooked patients, delivered in State Hospitals, were discharged without any screening or treatment, as occurred at this Institution. This reflects on midwives and doctors in the Labour ward who were seemingly unaware of the necessity for screening all unbooked patients and not discharging until results were known.

Although this study failed to show a correlation between unbooked status and positive syphilis serology, the prevalence of maternal syphilis at delivery (9%) is sufficiently high for staff to be aware of the chances of Congenital Syphilis occurring in infants born to unbooked mothers.

iii) The eighteen booked cases included untreated and inadequately treated patients. This scenario is a familiar one in many centres (8,11,14)

Five of the eighteen booked cases were inadequately treated during ANC. The "fault" lay with the patients who booked late in pregnancy and Health Workers' poor record-keeping. CDC defines "inadequate treatment" of Syphilis in Pregnancy, as any non-penicillin therapy or any penicillin therapy given within thirty days prior to delivery. (12) Treatment failures are associated with treatment in the month before delivery. (22) Meyer and Malan studied eighteen cases of maternal syphilis who were treated in the last month of pregnancy - including five who were treated with Erythrocin. Congenital Syphilis was diagnosed only in one infant, born to a mother who had received one dose of Penicillin eleven days prior to delivering. (16)

Although nine of the eighteen booked cases had documented positive serology, they had not been treated by the time of delivery. One of the important diseases which can be prevented by attending ANC is syphilis, yet in this study, for these patients, clinic attendance had little advantage over non-attendance. Delport notes that untreated maternal syphilis at delivery was previously anticipated in unbooked patients. However, studies at Kalafong showed that, in fact, more than 90% of their untreated seropositive patients had received antenatal screening. (19) In Swingler's retrospective study of twenty-seven infants with Congenital Syphilis, 78% of mothers booked late and by delivery 50% had received no treatment. (7)
Delay in results arriving back at antenatal clinic was one important reason for failure to initiate treatment. This is well-documented by Delport. (14,19,29) At the time of this study the cumbersome method of establishing RPR status (described in 5.1.4) was in operation at PHU and the MOU. The results were, theoretically, available within one week, i.e. at the patient's return visit. In practice, specimens and results were mislaid and patient-held ANC cards bearing results were left at home. "After hours" and during weekends, results could not be traced by staff and patients absconded when asked to wait for results of repeat screening tests.

The problem of poor patient compliance, such as defaulting STD treatment is a familiar one. On questioning patients as to the reasons why they did not attend for treatment, some complained about the "painful injections" and others were ashamed to be seen by friends and neighbours, entering the well-known STD clinic. At the MOU the STD clinic is in the same corridor as the antenatal clinic - the former staffed by LA nurses and the latter by CPA staff. Patients simply leave without visiting the STD clinic.

The various stages of breakdown in the process of antenatal prevention of Congenital Syphilis as described above are spelt out in the Khayelitsha study by Swingler. (7)

iv) Four of the thirty-four cases (12%) delivered at PHU had negative serology at their booking visit. In Manning's study of Syphilis in Pregnancy at King Edward VIII (23), 11.8% of patients who were seronegative at booking visits (<32 weeks gestation) tested positive at thirty-six weeks. Dorfman described seven infants with Congenital Syphilis in New York. The dramatic increase in the disease there is attributed to poor socio-economic conditions in prostitutes who are cocaine addicts. (24) At delivery four of the infants and their mothers had negative serology, while the other three mothers had negative syphilis serology during ANC, and had not been re-tested at delivery.
Since both mother and neonate are often asymptomatic, repeat RPR testing at delivery in high-risk areas should be undertaken. Issues such as the initial infection occurring late in pregnancy, seroconversion, false negative results, laboratory error, prozone effect, all play a role. (22) In many cases, maternal diagnosis of syphilis was made only when the infant presented with Congenital Syphilis. This is similar to the experience of Naiker et al (2) and Dorfman. (24)

Evidence of the areas where the Health System could be said to have failed must therefore be examined and corrected, viz:-

i) Patient booked
   - result not back by delivery, if ever;
   - result back, but patient not treated or not fully treated;
   - patient did not re-attend clinic.

ii) At delivery
   - patients with unknown RPR results not tested;
   - results known but previous treatment not checked;
   - known to be RPR positive and untreated, yet neither mother nor baby treated;
   - patient discharged before RPR available, therefore mother and baby untreated.

8.3.2 Neonatal Data

The greatest proportion of infants presented at an age of less than one month (19/40), but in the case of eleven patients the diagnosis was delayed to over the age of three months.
8.3.3 Serological Data

RPR titres of the babies ranged from 1:2 to 1:4096; confirmatory FTA-ABS test was recorded in twelve of the infants - IgG being positive in all cases, IgM positive in all but one case. The IgG was most likely a reflection of the mother's infection in the early stages of the disease and IgM indicated disease in the infant.

Serodiagnosis of Congenital Syphilis is known to be fraught with difficulty. (2,5,13,23)

CDC lists the specific "reactive test for FTA-ABS IgM Ab" as one of the diagnostic findings for Presumptive Congenital Syphilis in an infant with a "reactive Treponemal Test for Syphilis". This test is used overseas but is not available in South Africa. To date no perfect diagnostic test for Treponema Pallidum exists (22) TPHA and FTA-ABS however, are considered to be specific tests for syphilis.

The RPR screening test is a test for IgG and this test may be falsely negative in the neonate. This may be due to late infection or prozone phenomenon. Cord blood may give rise to false negative and false positive results and it is recommended that maternal venous blood be tested instead. (22) Falsely positive RPR may be due to a variety of causes including viral diseases, autoimmune response, tuberculosis. The titre is seldom > 1:8 in these instances.

In the neonate, a positive RPR test probably only means that the mother's RPR is positive. FTA-ABS test should be used to confirm the positive non-Treponemal test. Positive total IgM in neonatal blood suggests syphilis, because this is the commonest congenital infection - it may be positive in any congenital infection. A positive Specific IgM test is a clear indication that the infant has syphilis.

Abnormal CSF findings (VDRL positive, raised protein and leucocytes) also pose a diagnostic problem. The neonate has high protein and cell counts in CSF as compared to adults, but a normal CSF is no guarantee that the infant
does not have Congenital Syphilis. (22) In newborns some antibodies diffuse passively from serum into CSF and may give rise to a positive VDRL in CSF.

In this Hospital, lumbar punctures are not routinely done on cases of suspected Congenital Syphilis, for reasons given above. Despite the fact that the RPR titre in the newborn baby must be four times higher than the titre of the mother to confirm syphilis, in practice we rarely test the baby.

8.3.4 CDC recommends screening for syphilis at booking visit, last trimester and delivery in areas of high prevalence. Studies in Natal by Naiker et al (2) concluded that TPHA be used as a screening test and it should be repeated in the last trimester. They also suggest that "ideally" the FTA-ABS test should be performed on all infants born to mothers treated for Syphilis in Pregnancy. This is not supported by other authors: Ratnam et al advise RPR screening at diagnosis of pregnancy and again in late pregnancy (11); Delport supports the CDC recommendation (18); while Opai-Tetteh et al contest that the CDC recommendation is too costly for this country. (13) They advocate screening at booking visit and repeat testing at delivery. RPR screening of all patients at delivery will also ensure that unbooked patients are screened. The authors quoted above (13) do not give any indication of the actual projected costs at their institution nor do they indicate having performed cost studies.

8.3.5 Repeat screening of all patients at delivery at PHU and the MOU should ensure that the diagnosis of syphilis is not missed in the following categories:-

i) All unbooked patients;

ii) Booked patients with positive RPR at ANC who were untreated or inadequately treated by delivery;
iii) Booked patients with negative RPR at ANC who seroconverted and were RPR positive at delivery.

These categories accounted for 88% (30/34) of the cases in the Early Congenital Syphilis study.

8.3.6 The category of patient who would not be identified by the screening, is the one who contracted Syphilis in Pregnancy, and had not yet seroconverted. This patient would be RPR negative at delivery and her newborn infant asymptomatic. These cases numbered 4/34 (12%) of the patients in the study of Early Congenital Syphilis admissions. The patients were RPR negative at booking visit, and were not re-tested at delivery.

8.3.7 Retesting at delivery naturally will not prevent losses due to syphilitic stillbirths, or the birth of a syphilitic neonate. Prompt treatment at birth will serve to reduce morbidity and mortality due to syphilis.

8.3.8 It is to be hoped that, as staff become more aware of the problem by this enforced re-testing of all patients, the unbooked patients will all be screened, and the booked patients' records will be examined for details of treatment, if any. Once this state of affairs is achieved, the necessity for re-testing all patients will fall away.

8.3.9 As long as the prevalence of syphilis remains high, however, there will be some "missed" cases of Congenital Syphilis - the asymptomatic neonate of the patient with negative serology at ANC who seroconverts.
9. **RECOMMENDATIONS**

Since antenatal care is the key to the control of Congenital Syphilis, it must be of a high standard. In consultation with the midwives, the following changes have been proposed to the authorities at PHU. Some of the changes have already been partially applied.

9.1 **RPR results at first visit**

The existing inefficient system whereby all antenatal bloods were sent to EPBTS in Port Elizabeth for RPR, Group and Rh was abandoned. Whilst appreciating that “on site” screening as promoted by Delport (29) is the ultimate answer, a system closely approximating this has been employed. SAIMR at PHU has agreed to perform all RPR tests for antenatal clinics. Blood specimens are collected at 11 a.m. daily and printed results are available on the same day. Telephonic results can be obtained within two hours. Patients seen in the afternoons have to return the following day for results.

SAIMR are presently negotiating for a Satellite Laboratory at the Day Hospital which houses the MOU. A 24-hour service has recently been started at this Day Hospital and, in line with current thinking, SAIMR is keen to initiate this service, incorporating all basic tests.

9.2 **STD treatment initiated at ANC**

Patients with positive serology receive the initial 2.4mu Benzyl Penicillin at the antenatal clinic on the same day or the following day, depending on the time factor. They are asked to return within one week to the STD clinic (which is in the same passage), for two more weekly injections. Contacts are left to the STD staff to follow up. The initial dose of treatment effectively covers current or recent secondary syphilis when risk to the foetus is maximal. (7) Once “comprehensive” health care is available, the antenatal patient will receive all treatment at the antenatal clinic and the rate of non-compliance should be lower.
9.3 Patient Education

High prevalence of syphilis, teen pregnancies, non-attendance at ANC and late booking, all reflect the poor socio-economic background of the patients at PHU. This is huge problem especially as syphilis is often asymptomatic in mother and newborn baby. The increased susceptibility of these patients to HIV compounds the problem. Health Promotion and Health Education staff have an enormous task - to impact on knowledge, attitudes and practices of the population at risk. Countrywide AIDS campaign and Syndromic Approach to STD protocols will, hopefully, assist in resolving the issue.

9.4 Repeat RPR at delivery

Routine screening of all patients at delivery at PHU and the MOU is now performed, regardless of booking status. Maternal blood is tested, cord blood being no longer used because of the possibility of false negative and false positive results.

In the case of the booked patient who was treated antenatally, a rising titre in the repeat RPR alerts the Health Worker to the possibility of inadequate treatment or re-infection. The patient then receives further treatment and her infant is notified and treated according to clinical findings. Patients are not discharged from post-natal wards (or nursery) until print-outs of RPR results are delivered from SAIMR. Initial treatment is given, patients referred to STD Clinic, and HIV pre-counselling done as necessary. This system will be reviewed on a six-monthly basis. It is hoped that, by insistence on the repeat test, staff will become more aware of the prevalence and asymptomatic nature of syphilis in the patient at delivery and her newborn infant.
9.5 Treatment and Notification of Congenital Syphilis

The Infection Control Sister now oversees notifications in the hospital and ensures that slips are correctly completed and collected on a daily basis from her by LA.

CDC's "Surveillance Case Definition for Congenital Syphilis" proved to be confusing to Health Workers. This protocol was abandoned in favour of the policy guideline circular H90/1994 "Management of infants with or at risk of Congenital Syphilis" (Appendix III). Treatment and Notification guidelines set out in this document are much easier to follow.

Maternity and Casualty staff delivering stillborn infants have been alerted to the necessity of drawing maternal blood to ascertain the RPR status in all cases. The results are included in the folders and cases are notified by one dedicated nurse in Labour Ward who is responsible for all their statistics. All infants born to mothers with positive RPR at delivery are brought from the postnatal ward to the nursery. Treatment records, if any, are scrutinised and the baby examined by the Medical Officer on Paediatrics. The neonate is then notified and treated according to the guidelines above. Due to financial constraints, lack of space in the nursery and resistance from mothers, asymptomatic, well infants are notified and given one dose of Benzyl Penicillin 50,000u/kg and discharged. The infants are not admitted for ten days therapy even if the mother was untreated during pregnancy. The study by Radcliffe et al (25) although the numbers are small, supports the efficacy of single dose treatment in asymptomatic infants born to infected, untreated mothers with VDRL titres >1:16.

This is also policy in the Peninsula Maternal and Neonatal Services in Cape Town (Personal Communication - Dr David Greenfield).
In the instance of Low Birth Weight babies, they are often admitted in any case, for a variety of reasons and if they have positive syphilis serology, are usually treated with Procaine Penicillin 50,000u/kg for ten days. Mothers are satisfied that the weight gain is necessary before the infant can go home, usually to a zinc house in an informal sector. (Breast-feeding mothers at PHU have to pay for their own transport - about ten kilometres twice daily - as there are no facilities for "rooming in". Those who stay all day are given a midday meal from the ward.) Out-patient treatment would obviously not succeed in these conditions.

The ward secretary now "double checks" on notifications of stillbirths and neonatal deaths with Congenital Syphilis. Missed cases are quickly picked up since a new computer programme was introduced (see below 9.8).

9.6 "Active Notification"

This system, postulated by Coetzee (26) was initiated by SAIMR at PHU. Matron-in-charge of Maternity receives weekly print-outs of RPR results in all ANC clinics and Maternity ward. Names can then be checked to ensure that treatment has been initiated and notification done. The total number of patients with positive serology is now recorded, along with other statistics which are discussed at the monthly Obstetric-Paediatric meeting.

9.7 In-service Training of Health Workers

All Health Workers involved in maternity and paediatric care should undergo the distance training offered by the Perinatal Education Programme (PEP). At PHU the majority of the staff successfully completed the Newborn Course in 1995. Seemingly the findings of the Perinatal Mortality Study in Cape Province (28) prompted the PEP team to approach PHU management to suggest the programme.

All nursery protocols are based on this programme. It is hoped that the Maternal Care course will be embarked upon in the near future.
9.8 Evaluation

i) In January 1996, by kind favour of Dr D Greenfield, the Perinatal Problem Identification Programme (PPIP) was installed. Essential data to be entered includes booking status, RPR status and birth weight of all stillbirths and neonates. This ensures that these details are sought and recorded each month. Monthly statistics are discussed at a combined Obstetric/Paediatric meeting headed by the Obstetrician and attended by staff rotating through the two disciplines plus full-time maternity staff.

Since initiation of the PPIP, all private patients delivering at PHU have RPR status recorded as do all stillbirths weighing >500 grams. The number of PNM cases with RPR not done or unknown has shown a significant decline since the surveillance was inaugurated.

ii) An additional indicator supplied by the Ward Secretary is the total number of positive RPR patients delivering each month. This may be regarded as our own "active surveillance" scheme showing the trend of maternal syphilis in this hospital (see above 9.6). The prevalence rate for all titres, remains persistently over 10% of deliveries and this serves as a constant reminder to staff that at least one in ten patients has syphilis (and is probably in danger of being an HIV sufferer as well).

iii) The number of admissions of cases of Early Congenital Syphilis to the wards is the single most important indicator of the efficacy of the proposed changes. Each case is carefully studied to ascertain how and where the diagnosis was missed and individual members of staff are approached and questioned and given further training where appropriate.

iv) The question of sustainability of the proposed changes rests with the willingness of Health Workers to upgrade their skills. It is hoped that further launching of more "PEP" will ensure that this training is forthcoming.
10. CONCLUSION

Set in the "Cinderella" region - the East Cape - PHU serves a community with a poor socio-economic background. The high incidence of syphilis is reflected in the rate of syphilis at delivery - 19% for all titres, 9% for titres >1:8, and perinatal deaths due to syphilis - 10.8/1000 deliveries. The percentage of non-attendance at ANC is alarmingly high and urgent attention needs to be focused on this problem area.

This study highlighted the fact that failure to apply a high standard of care by Health Workers resulted in unbooked patients being discharged, either without screening or treatment, or before serology results were known. The asymptomatic nature of the disease was probably part of the reason. Booked patients' records were not assiduously examined to ensure that adequate and timeous treatment was administered prior to delivery. Neonates were discharged without ensuring that maternal RPR status was known, treatment administered and the disease notified. Patients who delivered stillborn infants were not checked for RPR status and notifications of syphilitic stillbirths were not performed. Protocols were not available, or used, for the management of suspected cases of Congenital Syphilis.

The existing system of serosurveillance for syphilis at ANC caused long delays in initiating treatment while the separation of ANC and STD clinics further added to the likelihood of delay or defaulting treatment.

Recommendations include:

i) The long-awaited social upliftment of this community;

ii) In-service training of Health Workers by PEP and availability of protocols of management;
iii) RPR results available without delay on a "same day" basis at ANC;

iv) Repeat RPR on all patients at delivery.

v) Monthly evaluation by PPIP and Multidisciplinary Meetings;

vi) A modicum of direct input and in-service training of staff at Level 1 and 2 Hospitals by the academic staff of our tertiary institutions.
REFERENCES


BIBLIOGRAPHY


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TO: 
REGIONAL HEADS
HEADS OF INSTITUTIONS
DISTRICT SURGEONS (PART- AND FULL TIME)

MANAGEMENT OF INFANTS WITH OR AT RISK OF CONGENITAL SYPHILLIS

1. The contents of the attached document have been accepted by the Branch as a policy guideline.

2. Please distribute to appropriate professional staff for implementation of the prescribed procedures.

Signed by candidate

signature removed
CLINICAL MANIFESTATIONS OF CONGENITAL SYPHILIS

Infants may be asymptomatic at birth or have only generalized signs of infection. Stillbirths and prematurity is relatively common. (Check placenta).

- Early manifestations are:
  - Palpebral due to thrombocytopenia.
  - Bone involvement presenting as lack of movement of limbs due to pain – pseudoparalysis.
  - Renal involvement presenting as nephrotic syndrome or glomerulonephritis.
  - Pneumonia.
  - Non-immune hydrops.

Hepatosplenomegaly ± neonatal jaundice. Anoeritic, oedema, lymphadenopathy.

MANAGEMENT

Both maternal VDRL (or NPI) and FTA (or TPHA) negative or only 1 positive

Mother has been fully treated (i.e., 3 x benzathine penicillin IM) before last month of pregnancy

Infant clinically well

No treatment, 

Infant has clinical signs of syphilis

Treat with procaine penicillin 50 000 Units/kg/day IM for 10 days (consecutively, if possible)

Infant asymptomatic

Treat with benzathine penicillin 50 000 Units/kg IM once only, 

Infant has clinical signs of syphilis

Treat with procaine penicillin 50 000 Units/kg IM once only, 

VDRL and FTA unknown

Determine maternal VDRL and then manage as for 'both VDRL & FTA positive'.

If not possible to wait for results of VDRL then treat clinically well infant with benzathine penicillin 50 000 Units/kg IM once only, but do not check results and treat infant fully if VDRL and FTA are positive.

Start treatment with procaine penicillin in any infant who has clinical signs of syphilis while waiting for the VDRL results.

DIAGNOSTIC TESTS FOR SYPHILIS

The only tests routinely used for the diagnosis of syphilis are VDRL or NPI (both are non-antireproliferative tests) and if either of these is positive a specific anti-syphilis test, e.g., FTA or TPHA is performed.

Any titre of VDRL or NPI is positive if the specific antireproliferative test is positive.

PRACTICAL POINTS

a) Allomucov Jacob for infection on IV-drip: Pen G 50 000 Units/kg 8 to 12 hourly IM for 10 days.

b) If infants stay too far from a local clinic or hospital to come for daily treatment, admission to hospital is necessary. Remember breast feeding promotion advice to mothers.

c) Still births and neonatal deaths due to congenital syphilis are notifiable.